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**Understanding the role of psychological factors in individuals with perceived food intolerance
an exploratory study**

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VOLUME I

SYSTEMATIC LITERATURE REVIEW
EMPIRICAL RESEARCH PROJECT

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LIST OF ABBREVIATIONS

FH	<i>Food hypersensitivity</i>
FA	<i>Food allergy</i>
PFI	<i>Perceived food intolerance</i>
QoL	<i>Quality of life</i>
GI	<i>Gastrointestinal</i>
CMD	<i>Common Mental Disorders</i>
IBS	<i>Irritable Bowel Syndrome</i>
FGID	<i>Functional Gastrointestinal Disorder</i>
IBD	<i>Inflammatory Bowel Disease</i>
DBPCFC	<i>Double-blind placebo-controlled food challenge</i>
CAM	<i>Complementary and Alternative Medicine</i>
GSA	<i>Gastrointestinal symptom-specific anxiety</i>
FR-QoL	<i>Food-related QoL</i>
CSM	<i>Common-sense model of self-regulation</i>
CBT	<i>Cognitive Behaviour Therapy</i>
ACT	<i>Acceptance and Commitment Therapy</i>

CHAPTER 1

SYSTEMATIC LITERATURE REVIEW

A SYSTEMATIC REVIEW OF PSYCHOLOGICAL,
CLINICAL AND PSYCHOSOCIAL CORRELATES OF
PERCEIVED FOOD INTOLERANCE

Alessandra De Petrillo, B.Sc., M.Sc.

Supervised by Dr Emma Godfrey and Dr Lyndsay Hughes

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Abstract

Background: Non-allergenic perceived food intolerance (PFI) is a distressing condition reported by up to 35% of individuals, whereas the prevalence of food allergy (FA) is 0.9 – 3%. The aim of the present paper is to systematically review the evidence for associated psychological, clinical and psychosocial factors in order to improve current understanding of PFI and contribute to future targeted interventions.

Methods: Articles published from 1970 until September 2019 were identified through Web of Science, Scopus, PsycINFO, MEDLINE, EMBASE and Global Health. Search terms involved PFI and various synonyms, combinations, operators, truncations, wild cards and limiters. Case-control, prospective cohort, cross-sectional and retrospective studies published in English that a) included a subject population of adults over 18 with PFI and b) examined psychological, clinical and/or psychosocial factors of PFI were reviewed in two stages against inclusion criteria, by three separate reviewers. The methodological quality was assessed, data were extracted, and a narrative synthesis was conducted.

Results: Of 2,627 abstracts identified, thirty-five articles met inclusion criteria and were reviewed. Data were predominantly reported at a cross-sectional level. The strongest evidence indicates female sex is associated with PFI. Studies consistently found individuals with PFI often report physical health complaints including gastrointestinal (GI) and extraintestinal symptoms, and GI and atopic conditions. Evidence indicating that psychological factors were significantly associated with PFI were inconsistent, though some evidence suggested increased levels of common mental disorders (CMD) and distress. Findings regarding psychosocial factors were mixed and sociodemographic data were infrequently collected.

Conclusions: PFI is associated with female sex and gastrointestinal and extraintestinal complaints. Limited high-quality evidence supports the role of psychological factors in self-reported PFI. High-quality research using prospective and longitudinal designs with multivariate analyses is needed. Future research should explore modifiable psychological factors as potential targets for intervention, and to identify clinical and psychosocial risk factors of PFI to aid in formulating a biopsychosocial model of PFI.

1 Introduction

1.1 Background

Food hypersensitivity represents an area of marked interest in the public domain yet remains a challenge for health care professionals and patients alike, with widespread associated personal and social costs. The experience is distressing, and symptoms can range from gastrointestinal (GI) discomfort to life-threatening immunological response (Johansson et al., 2001; Muraro et al., 2014; Skypala, 2011). For many, the unpredictable nature of symptoms, diagnostic challenges faced by healthcare professionals, and wide range of associated symptoms lead to repeated healthcare visits which increases economic burden, self-diagnosis, food avoidance, increased psychological distress, and reduced quality of life (Fox et al., 2013; Gupta et al., 2010; Hazeldine, Worth, Levy, & Sheikh, 2010; Jones & Burks, 2017; Lieberman & Sicherer, 2011; Nelson & Ogden, 2008).

1.2 Definitions and Prevalence

Immune-mediated food allergy (FA) is predominantly cell-mediated or antibody-mediated. Immediate and recognisable allergenic symptoms include; itching or burning in the mouth and throat, swelling and throat constriction, or in severe reactions; anaphylactic shock following ingestion, airborne inhalation or skin contact with the allergen (Muraro et al., 2014; Ortolani & Pastorello, 2006; Sicherer & Sampson, 2014). Non-allergic reactions are typically mediated through 'enzymatic, pharmacological and additional undefined' mechanisms (Ortolani & Pastorello, 2006; Sicherer & Sampson, 2014; Zopf, Baenkler, Silbermann, Hahn, & Raithel, 2009). Associated symptoms are typically delayed, and include GI symptoms of bloating, changes in bowel movements (constipation or diarrhoea), pain and discomfort, and extraintestinal symptoms including fatigue, migraines, headaches, and joint pain, or any of these symptoms in combination (Kelsay, 2003; Ortolani & Pastorello, 2006; Sicherer & Sampson, 2014).

The terms 'food sensitivity', 'food hypersensitivity', 'food intolerance', 'food allergy' and adverse 'food reactions' are often used interchangeably, contributing to confusion for practitioners and public alike. A position statement from the European Academy of Allergy and Clinical Immunology (EAACI) recommended 'hypersensitivity' as

the umbrella term for both allergic and non-allergic reactions (Johansson et al., 2001), yet definitions and recommended terminology of ‘food allergy’ and ‘food intolerance’ have been proposed by the US National Institute of Allergy and Infectious Diseases (NIAD) (Sicherer & Sampson, 2018). In the current systematic review, ‘perceived food intolerance (PFI)’ will be used to describe nonimmune hypersensitivity reactions that are self-reported by individuals, ‘food allergy (FA)’ will be used to describe immune-mediated hypersensitivity reactions, and ‘food hypersensitivity (FH)’ will be used as an umbrella term where appropriate.

FH is self-reported by up to 35% of the general population, though clinically-confirmed FA is only established in 0.9 – 3% of adults (Muraro et al., 2014; Nwaru et al., 2014; Rona et al., 2007; Woods et al., 2002; Zuberbier et al., 2004). Though outside the scope of this review, evidence indicates that prevalence of FH and related hospital admissions is increasing (Gupta, Sheikh, Strachan, & Anderson, 2007; Nwaru et al., 2014; Prescott & Allen, 2011; Sicherer & Sampson, 2014, 2018), though research has additionally demonstrated incidence is not increasing (McGowan, Peng, Salo, Zeldin, & Keet, 2016; Nwaru et al., 2014). There is a significant discrepancy in prevalence between PFI and FA though true estimates are difficult to attain due to diagnostic challenges (Turnbull, Adams, & Gorard, 2015), and it is difficult to know whether reported rise in prevalence is due to an actual increase in FH, or increased awareness and self-reporting.

1.3 Impact and Correlates of PFI

Research investigating correlates of PFI is limited, though evidence suggests PFI is more often reported in women (Knibb et al., 1999; Lillestøl et al., 2010) and in those who meet criteria for Irritable Bowel Syndrome (IBS) (Atkinson, Sheldon, Shaath, & Whorwell, 2004; Dainese, Galliani, Lazzari, Leo, & Naccarato, 1999; Lind et al., 2005; Lind, Berstad, Hatlebakk, & Valeur, 2013; Lind, Lied, Lillestøl, Valeur, & Berstad, 2010; Lind, Lillestøl, et al., 2010; Monsbakken, Vandvik, & Farup, 2006). IBS is a functional GI disorder (FGID) where, despite absence of organic pathology, symptoms persist and cause functional impairments and distress (Drossman, 2016; Morton, Elliott, Cleland, Deary, & Burton, 2017; Rosendal et al., 2017; Windgassen et al., 2017). Psychological and psychosocial

factors can interact with biological factors to precede and precipitate IBS and may also contribute to perpetuating symptoms (Sibelli et al., 2016). IBS is associated with trauma, adverse early experiences, life stress, anxiety, depressive and somatoform disorders, and elevated symptoms of depression and anxiety compared to controls without IBS (Fond et al., 2014; Shah, Rezaie, Riddle, & Pimentel, 2014; Videlock et al., 2009; White et al., 2010; Whitehead, Palsson, & Jones, 2002).

Psychological factors in PFI have not been as thoroughly investigated, though suggest that distress may be a characteristic feature. Lillestøl et al. (2010) reported 57% of individuals with PFI met criteria for any psychiatric disorder, which is above the reported population prevalence of common mental disorders (CMD) including depressive disorders and anxiety disorders in England, which is around one in six (Bebbington & McManus, 2020). Additionally, research in PFI indicates self-reported increased anxiety, depression and somatic symptoms compared to controls (Knibb et al., 1999; Lillestøl et al., 2010; Lind et al., 2005), though the study designs used and analyses conducted preclude determining the direction of the relationship, and the findings are difficult to generalise to the wider population. PFI carries social implications, and perceived negative evaluations from others appear to be important. Qualitative research from Nettleton, Woods, Burrows, and Kerr (2010) highlighted an emotional impact of not having an authentic 'illness identity' and related experiences of increased anxiety, uncertainty and negative perceptions from others as there is no 'explanation' for PFI.

A lack of a clear understanding of PFI is problematic for diagnosis and management (Nettleton et al., 2010), which may contribute to reported distress. Qualitative research additionally suggests general practitioners hold a strong association between food intolerance and psychological distress (Nelson & Ogden, 2008). This may impact how medical professionals perceive their patients' complaints, and communicate with patients with PFI, though this is not known. However, communication in the doctor-patient relationship has been demonstrated to be important in IBS (Halpert & Godena, 2011).

The beliefs an individual holds about their condition, known as illness perceptions, can directly influence their cognitive and emotional response and subsequent coping and

management strategies (Petrie & Weinman, 2006; Leventhal, 1984; Leventhal, Phillips, & Burns, 2016). Symptoms in PFI are attributed to food, and specific thoughts and beliefs can increase attention towards information in line with the belief (Brosschot, 2002), which might perpetuate PFI-related beliefs, though this is not known. PFI poses challenges for psychological, social and health-related well-being, however, little is known about the role of psychological, clinical, and psychosocial factors associated with PFI.

PFI is not well understood, and it is important to rigorously consider the evidence for psychological, clinical and psychosocial correlates of PFI to better understand this condition including its sequelae and potential risk factors. There are similarities between PFI and IBS, and it is possible that these represent similar conditions, however, this is not known. It is important to identify factors that are significant in PFI, as these may contribute to outcome, including managing symptoms and the psychological impact of PFI. Enhancing our understanding is necessary in order to conceptualise PFI using a biopsychosocial model, whereby symptoms can be understood to occur from an interaction of genetic and environmental vulnerabilities, psychological and psychosocial factors. This can inform which modifiable correlates are necessary to address in a future successful intervention to help individuals manage PFI.

1.4 Rationale and Aims

It is likely that in PFI, symptoms are the result of multiple interactions, however, current understanding is limited by a paucity of data specifically exploring factors associated with PFI, and a lack of high-quality evidence to draw from. To the authors knowledge, there has been no previous systematic review examining the evidence for correlates of PFI, and it is hoped that the results of this review can help to further the current understanding of people with PFI. The ability to identify modifiable psychological correlates in addition to associated clinical and psychosocial factors can contribute a greater understanding of PFI for the public and medical professionals alike and can help advance evidence-based and theory-informed interventions to improve outcomes, as has been demonstrated in IBS.

The current review aims to systematically identify and evaluate the existing literature for evidence of (a) modifiable psychological correlates that are associated with PFI, as primary objectives, (b) and clinical or psychosocial correlates that are associated with PFI, as secondary objectives. For the purpose of this review, psychological variables were defined as those related to emotions, beliefs and attitudes which could potentially be modified in treatment, trait characteristics such as personality, and psychosomatic variables. Clinical factors were defined as comorbid physical health conditions. Psychosocial factors were defined as demographic and socioeconomic factors.

2 Methods

2.1 Search Strategy

The systematic review protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO; ID: CRD42019122826) and was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher, Liberati, Tetzlaff, Altman, & Group, 2010). Electronic databases (Web of Science, Scopus, PsycINFO, MEDLINE, EMBASE and Global Health) were systematically searched from 1970 to September 23, 2019 by the first author (A.D.), and two independent reviewers (S.M.) and (D.R.). Reference lists of articles meeting inclusion criteria were hand-searched for additional relevant studies. Search terms involved combining key word searches for perceived food intolerance using various synonyms, combinations, operators, truncations, wild cards and limiters and terms were selected to identify studies on PFI and reduce capturing those on FA. For example, food intolerance was searched for by the key words (“food intolerance” or “food hypersensitiv*” or “food sensitiv*”) and perceived was searched for using the key words (“perceived” or “self-report*” or “self report*” or “subjective”). As this is an understudied area, the decision was made to only use these terms, and manually screen out studies that did not meet criteria. See Appendix I for further details of the PRISMA checklist, and Appendix II for the search strategy.

Inclusion Criteria <i>PICOS inclusion criteria</i>	Exclusion Criteria <i>PICOS exclusion criteria</i>
<ul style="list-style-type: none"> (i) Subject population included adults >18 who self-reported PFI. (ii) Any comparators to be included (iii) Descriptive study designs (except those excluded) including case control, prospective, cohort, retrospective, and cross-sectional studies with n = >5 participants. (iv) Examined psychological, clinical and/or psychosocial factors associated with perceived food intolerance <p>To guide the selection of appropriate studies, factors that were deemed relevant included;</p> <ul style="list-style-type: none"> (i) Psychological factors including affect, CMD and/or distress, information relating to beliefs or cognitive patterns; personality traits; symptoms and symptom severity (ii) Clinical factors including self-reported and confirmed diagnoses (iii) Psychosocial factors including demographic and socioeconomic information 	<ul style="list-style-type: none"> (i) Caregivers; or children and adolescents under 18 where data was not separated (ii) Medically diagnosed nut allergy and anaphylactic allergy (iii) Individuals with a diagnosis of Coeliac Disease or Inflammatory Bowel Disease (iv) Focus on food additives such as sulphite, food colouring, or alcohol intolerance, as this was not the aim of the current review (v) Only included prevalence information (with no additional psychological, clinical or psychosocial information), or an outcome of PFI (including food/nutrient intake, dietary patterns or changes, diet adherence, pathophysiological changes, and impact on quality of life) (vi) Any of the following study designs: intervention study, outcome study, randomised controlled trial, replication study, study abstract, single-N case study, letter, consensus statement, incomplete report, book chapter, theses and reviews.

Table 1

'a priori' PICOS Screening Table

2.2 Study Screening and Selection

Articles identified in the initial search strategy were screened in two stages following inclusion and exclusion criteria, by the three independent reviewers (A.D., S.M and D.R.). When necessary, disagreements were resolved through a discussion with a fourth independent reviewer (E.G./L.H.). Identified papers were examined for duplicates and initially screened by title and abstract. The second stage involved reviewing full-text articles for relevance and inclusion using PICOS criteria and an *a priori* screening table (see Table 1). Where the full text was not available, attempts to contact study authors

were made. Inter-rater agreement was assessed using Cohen's Kappa. At the abstract screening stage, Cohen's Kappa was 0.78 between A.D. and S.M., and 0.82 between A.D. and D.R. At the full-text stage, Cohen's Kappa was 0.80 between A.D. and S.M. and 0.76 between A.D. and D.R.

2.2.1 Inclusion Criteria

Studies were included if they had (i) a subject population of adults >18 who self-reported PFI, (ii) descriptive study designs including case control, prospective, cohort, retrospective, and cross-sectional studies with N = > 5 participants, (iii) any comparators, and (iv) examined psychological, clinical and/or psychosocial factors associated with PFI. To guide the selection of appropriate studies, factors that were deemed relevant included; (i) Psychological factors including affect, CMD and/or distress, information relating to beliefs or cognitive patterns; personality traits; symptoms and symptom severity (ii) Clinical factors including self-reported and confirmed diagnoses (iii) Psychosocial factors including demographic and socioeconomic information.

2.2.2 Exclusion Criteria

Studies were excluded if they had (i) a subject population including caregivers, children and/or adolescents <18 where data were not reported separately, individuals with medically diagnosed nut or anaphylactic allergy, Coeliac Disease or Inflammatory Bowel Disease, and/or a food additive or alcohol intolerance, (ii) study designs including intervention, outcome, replication, single-N case studies, randomised controlled trials, study abstracts, letters, consensus statements, incomplete reports, book chapters, theses and reviews; (iii) only included prevalence information (with no additional psychological, clinical or psychosocial information), or an outcome of PFI (including food/nutrient intake, dietary patterns or changes, diet adherence, pathophysiological changes, and impact on quality of life).

2.3 Data Extraction and Synthesis

Information deemed relevant to the review question was extracted and tabulated by three reviewers (A.D., S.M. and D.R). Extracted data included publication data, country of origin, study design, recruitment method, sample characteristics, data analysis methodology, data collection methodology (including any outcome measures used), and main findings related to psychological variables, clinical variables, and psychosocial variables. The reporting of summary measures were not possible and a meta-analysis was not conducted due to the heterogeneity of data from included studies and broad research question. A narrative synthesis was conducted (Campbell et al., 2020), and data specific to psychological, clinical, and psychosocial factors were conceptually organised.

2.4 Quality Assessment

Methodological quality of each study included was assessed by three reviewers (A.D., S.M. and D.R) using adapted criteria from the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies ("Effective Public Health Practice Project," 1998a; "Effective Public Health Practice Project," 1998b). This instrument was developed in order to support the quality of systematic reviews and assesses the methodological quality of an article across eight areas of potential bias, including A) selection bias; B) study design; C) confounders; D) blinding; E) data collection method, F) withdrawals and dropouts G) intervention integrity and H) analysis. The EPHPP then rates the article as 'strong', 'moderate' or 'weak' on components A-F, which are used to determine the global rating. The current review did not include criteria concerning blinding (D) or intervention integrity (G), as we did not include controlled trials or intervention studies. Each article included was rated on five areas of potential bias: selection bias; study design; confounders; data collection method, and withdrawals and dropouts (see Appendix III for the adapted EPHPP used in the current review). Scores from each section translate into an overall methodological quality score of 'Strong' (no ratings of 'weak'), 'Moderate' (one rating of 'weak') or 'Poor' (two or more ratings of 'weak'). There was an agreement rating of 80% between A.D. and S.M, and 78% between A.D. and

D.R. regarding the global ratings of methodological quality. All discrepancies were resolved through discussion with a fourth independent reviewer (E.G./L.H.).

3 Results

3.1 Results of the Search

A total 2,627 articles were identified through the initial electronic database search. The hand-search yielded 3 additional articles, which were excluded. 683 duplicates were removed, and 1944 papers were screened. 145 papers were eligible for full-text review, of which 110 did not meet eligibility criteria. The most common reason for exclusion was incorrect target population, followed by type of publication (e.g. study design or publication such as conference abstract). 35 articles were included in the final review. Figure 1 presents the PRISMA flow diagram for the selection and inclusion process.

3.2 Study Characteristics

3.2.1 Overview of Studies

The characteristics of included studies and their samples are presented in Table 2. Thirty-five articles, including a total of 167,663 participants were eligible for inclusion. Sample sizes ranged from 43 (Rix, Pearson, & Bentley, 1984) to 64,316 participants (Jakobsen, Braaten, Obstfelder, & Abelsen, 2016) and the median sample size was 427 (IQR = 129 - 2251). Participants were recruited from 24 countries including Korea, Hungary, Sweden, Argentina, Netherlands, Norway, Mexico, Canada, Iceland, France, Australia, Italy, Turkey, Iran, Germany, United Kingdom, Finland, Japan, USA, Belgium, Switzerland, Ireland, Spain, and New Zealand. Most studies (83%) were cross-sectional ($n = 29$), with remaining studies of case-control ($n = 5$) or longitudinal ($n = 1$) designs. Statistical analyses were predominantly descriptive, inferential and bivariate, and few studies used multivariate analyses including regression and mediation analyses. Included studies were conducted within clinical ($n = 15$), community ($n = 12$), and population-based ($n = 8$) settings. Three studies investigated wheat and/or gluten intolerance (PFI-G) and five studies investigated lactose intolerance (PFI-L).

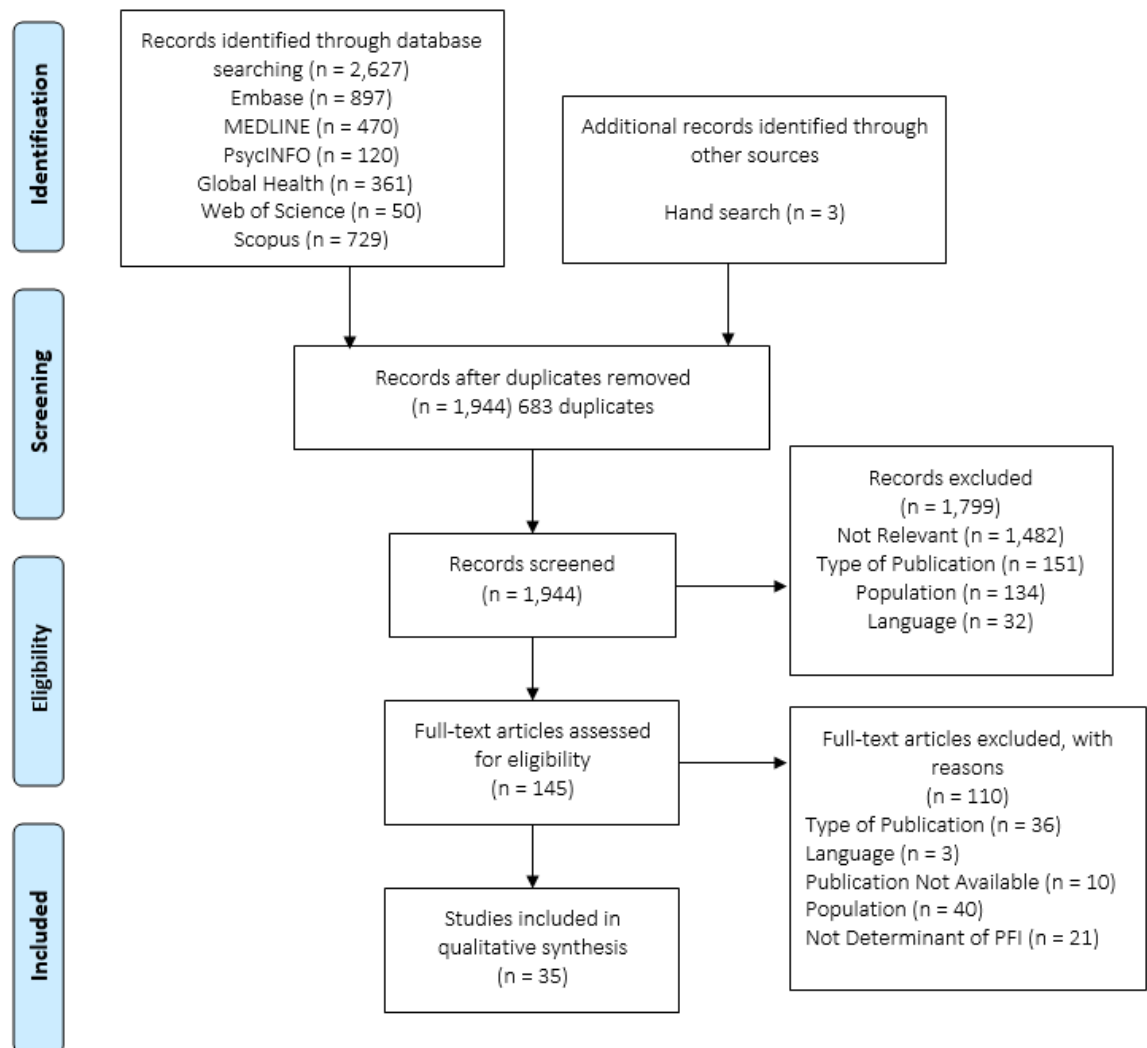


Figure 1. PRISMA flow diagram (Moher et al., 2010)

3.2.2 Sample Characteristics

Sample characteristics are presented in Table 2. The age of participants ranged from 18 – 90, and the median age across studies is 40.3 (IQR = 35 – 47). Nine studies did not report sample age, of which three did not report sample characteristics (Barr, 2013; Gelincik et al., 2008; Jansen et al., 1994; Lee et al., 2019; Liden, Kristjansson, Valtysdottir, Venge, & Hllgren, 2010; Patten & Williams, 2007; Rentzos, Johanson, Sjolander, Telemo,

& Ekerljung, 2015; Soost et al., 2009; Vierk, Koehler, Fein, & Street, 2007). There was a global trend of a high proportion of female participants, and the median of percentage of females is 68.5% (IQR= 55 – 79).

Nine studies were national/population based. Seven studies were community-based, of which three were comprised of populations from previously defined cohort studies (Jakobsen et al., 2016; Patelis et al., 2014; Woods, Abramson, Bailey, & Walters, 2001). Fifteen studies were comprised of outpatients recruited from gastrointestinal, allergy, and medical outpatient departments, including patients with gastrointestinal conditions (n = 5), PFI (n = 8), Rheumatoid Arthritis (n = 1), and Chronic Fatigue (n = 1).

3.2.3 PFI Characteristics: Prevalence, Offending Foods and Common Symptoms

In population-based studies, prevalence ranged from 7.3% (PFI-G) (Golley, Corsini, Topping, Morell, & Mohr, 2015) to 9.5% (Gelincik et al., 2008). In a population study, Monsbakken et al. (2006) reported a PFI prevalence of 70% however, this study only included respondents who reported IBS with ‘alarm symptoms’, thus was not representative of the general population. In community studies, PFI prevalence ranged from 6.2% (PFI-G) (van Gils et al., 2016) to 51.2% (Elieson, Domotor, & Koteles, 2017). In clinical samples (excluding PFI outpatient samples), PFI was reported by 19% (Nybacka et al., 2018) to 84% (Bohn, Storsrud, Tornblom, Bengtsson, & Simren, 2013) of IBS outpatients, 13.5% of patients with Chronic Fatigue (Manu, Matthews, & Lane, 1993) and 27% of those with Rheumatoid Arthritis (Liden et al., 2010).

Table 2

Study Characteristics

Author (year)	Country	N	Diagnostic Status	Age (M±SD/Range)	Female (%)	Setting Study Design	PFI & Prev. %	Measures
1. Barr, S. I. (2013)	Canada	2251	N/S	NR	48.5%	Population-based <i>Cross-Sectional</i>	PFI-L 16.3%	MHBS
2. Berstad, A., et al. (2012)	Norway	84	PFI	37 (Range:1 8-77)	68%	Dept. of Medicine <i>Cross-Sectional</i>	PFI 100%	FFS, IBS-SSS
3. Bohn, L., et al. (2013)	Sweden	197	IBS	35.3 (±11.9)	72%	GI Dept. patients <i>Cross-Sectional</i>	PFI 84%	HADS, VSI, PHQ-15, IBS-SSS
4. Cabrera-Chavez, F., et al. (2017)	Argentina	1209	N/S	30 (Range:1 8-84)	52.4%	Community <i>Cross-Sectional</i>	PFI-G 7.61%	
5. Dainese, R., et al. (2014)	France	51	IBS	45 (±16)	80.4%	GI Dept. patients <i>Cross-Sectional</i>	PFI-L 41%	HADS, BDI
6. Elieson, L. M., et al. (2017)	Hungary	335	N/S	35.1 (±13.8)	75.8%	Community (online) <i>Cross-Sectional</i>	PFI 51.2%	SHAI, MHW, SSAS, HCAMQ
7. Gelincik, A., et al. (2008)	Turkey	11816	N/S	NR	72.9%	Population-based <i>Cross-Sectional</i>	PFI 9.5%	
8. Golley, S., et al. (2015)	Australia	1184	N/S	51.6 (±16.8)	52.9%	Population-based <i>Cross-Sectional</i>	PFI-G 7.3%	Medical History, NEO-N, WI
9. Hidese, S., et al. (2019)	Japan	11876 1000 10876	Total Depression Control	41.4 (±12.3)	49.9%	Community (online) <i>Cross-Sectional</i>	PFI 14.5%	K6
10. Jakobsen, M. D., et al. (2016)	Norway	64316	N/S	56.1 (Range:4 1-76)	100%	NOWAC sample <i>Cross-Sectional</i>	PFI 6.8%	Medical History
11. Jansen, J. J. N., et al. (1994)	Netherlands	1483	N/S	NR	65%	Housing register <i>Cross-Sectional</i>	PFI 13.35%	
12. Knibb, R. C., et al. (1999)	UK	535	N/S	48 (Range:1 8-90)	55%	Community sample <i>Cross-Sectional</i>	PFI 24%	GHQ-28, EPQ
13. Lee, H. J., et al. (2019)	Korea	393 101 167 125	Total IBS GI/No-IBS Control	NR	NR	GI clinic outpatients <i>Cross-Sectional</i>	PFI 44.8%- 79.2%	IBS-SSS
14. Liden, M., et al. (2010)	Sweden	241	Rheumatoid Arthritis	NR	83%	Dept. of Rheumatology <i>Cross-Sectional</i>	PFI 27%	
15. Lillestol, K., et al. (2010)	Norway	205 130 75	Total PFI Matched controls	39.5 (Range: 18-80)	82.3%	Clinical Allergology <i>Case-Control</i>	PFI 100%	MINI, HADS, MADRS, GHQ-30, EPQ-N
16. Lind, R., et al. (2005)	Norway	166 56 50 70	Total PFI Healthcare Workers Matched Controls	39 (Range: 19-80)	89%	Allergy clinic <i>Case-Control</i>	PFI 100%	SHC, MHW

Author (year)	Country	N	Diagnostic Status	Age (M±SD/Range)	Female (%)	Setting Study Design	PFI & Prev. %	Measures
17. Lind, R., et al. (2008)	Norway	116 46 70	Total PFI Matched Controls	40.6 (Range:19-80)	89%	Allergy clinic <i>Case-Control</i>	PFI 100%	
18. Lind, R, Lied, G et al. (2010)	Norway	70	PFI	39.2 (Range:18-75)	74%	Allergy & GI clinic <i>Cross-Sectional</i>	PFI 100%	HADS, VSI, SHC, IBS-SQ
19. Lind, R., Lillestol, K. et al (2010)	Norway	129 64 65	Total PFI Matched Controls	37.9 (±11.7)	83%	Allergy & GI clinic <i>Case-Control</i>	PFI 100%	SHC, CJSQ, UCL
20. Manu, P., et al. (1993)	USA	200 27 27	CFS PFI+CFS Matched CFS	40.0 (±6.5)	64%	Medical clinic <i>Case-Control</i>	PFI 13.5%	NIMH-DIS
21. Monsbakk en, K. W., et al. (2006)	Norway	84	IBS	48.5 (±15)	69%	National Health Survey; Population-based <i>Cross-Sectional</i>	PFI 70% with IBS	HSCL-10, Musculoskeletal Quest.
22. Nybacka, S., et al. (2018)	Sweden	270 223 47	Total IBS Control	31 (Range:18-72)	74%	GI clinic <i>Cross-Sectional</i>	PFI 19%	HADS, PHQ-15
23. Parker, S. L., et al. (1990)	Canada	45 23 22	Total PFI FA	41.5 (± 9.6)	91.3%	Allergy clinic <i>Cross-Sectional</i>	PFI 100%	
24. Patelis, A., et al. (2014)	Iceland & Sweden	2307	ECRHS I & ECRHS II	33.6 (±7.3) 42.4 (±7.2)	53%	ECRHS sample <i>Longitudinal</i>	PFI 20.6%	
25. Patten, S. B. & J. V. Williams (2007)	Canada	36984	N/S	NR	NR	Canadian Community Health Study; Population-based <i>Cross-Sectional</i>	PFI 8.2%	WMH-CIDI
26. Puente-Fernandez, C., et al. (2016)	Mexico	1253	N/S	19 (Range:18-25)	58.2%	Community <i>Cross-Sectional</i>	PFI 30.1%	
27. Rentzos, G., et al. (2015)	Sweden	1527	WSAS	NR	NR	West Sweden Asthma Study; Population-based <i>Cross-Sectional</i>	PFI 53.1% with asthma	
28. Rix, K. J., et al. (1984)	UK	43 23 20	Total PFI Psych.	40.8 (Range:21-67)	65%	Allergy & Psych. <i>Cross-Sectional</i>	PFI 100%	CIS, SRT
29. Saberi-Firoozi, M., et al. (2007)	Iran	1978	N/S	49.9 (±11.14)	70.7%	Population-based <i>Cross-Sectional</i>	PFI-L 28.4%	
30. Soost, S., et al. (2009)	Germany	3227	N/S	NR	55.6%	Population-based <i>Cross-Sectional</i>	PFI	
31. Tomba, C., et al. (2012)	Italy	114 102 12	Total GI Control	42 (±15)	72%	GI outpatients <i>Cross-Sectional</i>	PFI-L 29%	SCL-90R

Author (year)	Country	N	Diagnostic Status	Age (M±SD/Range)	Female (%)	Setting Study Design	PFI & Prev. %	Measures
32. van Gils, T., et al. (2016)	Netherlands	785	N/S	47 (±18)	60%	Community Cross-Sectional	PFI-G 6.2%	Medical History
33. Vesa, T. H., et al. (1998)	Finland	427	N/S	52 (Range 36-74)	52%	Community Cross-Sectional	PFI-L 31%	
34. Vierk, K. A., et al. (2007)	USA	4482	N/S	NR	61.2%	Population-based Cross-Sectional	PFI 9.1%	
35. Woods, R. K., et al. (2001)	Australia Data from 15 countries	17280	ECRHS	33.2 (±7.2)	52%	ECRHS sample; Community Cross-Sectional	PFI 12.2%-19.9%	
<p>BDI = Beck Depression Inventory; CIS = Clinical Interview Schedule; CJSQ = Cooper's Job Stress Questionnaire; EPQ = Eysenck Personality Questionnaire; FFS = FibroFatigue Scale; HADS = Hospital Anxiety Depression Scale; HCAMQ = Holistic Complementary and Alternative Medicine Questionnaire; HSCL-10 = Hopkin Symptom Check List 10; IBS-SQ = IBS Symptom Questionnaire; IBS-SSS = IBS Severity Scoring System; K6 = Kessler 6-item Scale; MADRS = Montgomery-Åsberg Depression Rating Scale; GHQ = General Health Questionnaire (28 and 30); MHBS = Milk Health Beliefs Scale; MHW = Modern Health Worries; MINI = Mini International Neuropsychiatric Interview; NEO = NEO Personality Inventory; NIMH-DIS = National Institute of Mental Health Diagnostic Interview Schedule; PHQ-15 = Patient Health Questionnaire; SCL-90 = Symptom Checklist 90; SHAI = Short Health Anxiety Inventory; SHC = Subjective Health Complaints Inventory; SRT = Symptom Rating Test; SSAS = Somatosensory Amplification Scale; UCL = Utrecht Coping List; VSI = Visceral Sensitivity Index; WI = Whitely Index; WMH-CIDI = World Mental Health Composite International Diagnostic Interview;</p> <p>Legend: N/S = no diagnostic status; NR = not reported; PFI = Perceived Food Intolerance; IBS = Irritable Bowel Syndrome; GI = gastrointestinal; CFS = Chronic Fatigue Syndrome</p>								

Commonly reported offending foods were wheat, gluten, dairy (including milk and cheese), fruits, vegetables (including legumes and cruciferous vegetables), and eggs. Individuals with PFI often reported symptoms in response to more than one food (Bohn et al., 2013; Elieson et al., 2017; Lee et al., 2019; Lind et al., 2005; Lind, Olafsson, Hjelland, Berstad, & Lied, 2008; Monsbakken et al., 2006; Nybacka et al., 2018), and one study indicated that women reported more food items than men (Bohn et al., 2013). The most commonly reported GI symptoms were bloating, flatulence, abdominal discomfort, abdominal pain, nausea, altered bowel habits (constipation and/or diarrhea). The most commonly reported extraintestinal symptoms were tiredness, headache, joint/muscle pain, and mood changes.

3.3 Methodological Quality Assessment

Results from the quality assessment are presented in Table 3 and Figure 2. Table 3 depicts individuals quality ratings for each included article, and Figure 2 demonstrates percentage proportions of component ratings and global rating across all articles. Overall, 11.4% (n = 4) of articles received a global rating of 'Strong', 40% (n = 14) of 'Moderate', and 48.6% of 'Weak' (n = 17).

According to EPHPP criteria, most studies were subject to selection bias, largely due to consecutive and convenience sampling methods by means of self-selection or clinic referrals, and thus might not be representative of the general population. Eight studies used probability sampling methods including random digit dialing and postal questionnaires (Barr, 2013; Gelincik et al., 2008; Golley et al., 2015; Monsbakken et al., 2006; Patten & Williams, 2007; Saberi-Firoozi et al., 2007; Soost et al., 2009; Vierk et al., 2007), however this resulted in lower response rates, contributing to 'moderate' and 'weak' ratings. Study design was a primary area of bias in 29 studies, who received ratings of 'weak' due to their cross-sectional design, which does not allow for variables of interest to be measured over time, and many did not account for confounding or extraneous variables that may have influenced psychological or clinical correlates. Six articles received a rating of 'moderate' on study design; five employed a case-control design with age- and sex-matched controls (Lillestøl et al., 2010; Lind et al., 2005; Lind, Lillestøl, et al., 2010; Lind et al., 2008; Manu et al., 1993) which can reduce the chance that findings were due to uncontrolled variables, and one employed a longitudinal design (Patelis et al., 2014). Sixteen studies used known reliable and valid measures, though most validated measures used were self-report, which may be prone to biases in reporting due to their subjective nature. As most studies were one-time survey studies, EPHPP criteria indicates that the withdrawal and dropout component is not applicable for these studies and was only relevant in one longitudinal study.

Table 3

Adapted EPHP Quality Assessment Ratings for Each Study

Author (year)	Selection Bias	Design	Confounders	Data Collection	Withdrawals	Global Score
Barr, S. I. (2013)	-	-	X	+	X	-
Berstad, A., et al. (2012)	+	-	X	+	X	+
Bohn, L., et al. (2013)	+	-	X	++	X	+
Cabrera-Chavez, F., et al. (2017)	-	-	X	+	X	-
Dainese, R., et al. (2014)	+	-	X	++	X	+
Elieson, L. M., et al. (2017)	-	-	-	-	X	-
Gelincik, A., et al. (2008)	+	-	X	+	X	+
Golley, S., et al. (2015)	-	-	X	-	X	-
Hidese, S., et al. (2019)	-	-	-	++	X	-
Jakobsen, M. D., et al. (2016)	+	-	X	+	X	+
Jansen, J. J. N., et al. (1994)	+	-	X	-	X	-
Knibb, R. C., et al. (1999)	-	-	X	++	X	-
Lee, H. J., et al. (2019)	+	-	-	++	X	-
Liden, M., et al. (2010)	-	-	-	-	X	-
Lillestol, K., et al. (2010)	+	+	++	++	X	++
Lind, R., et al. (2005)	+	+	++	+	X	++
Lind, R., et al. (2008)	+	+	++	-	X	+
Lind, R., Lied, G., et al. (2010)	+	-	X	++	X	+
Lind, R., Lillestol, K. et al. (2010)	+	+	++	-	X	+
Manu, P., et al. (1993)	+	+	++	++	X	++
Monsbakken, K. W., et al. (2006)	+	-	X	++	X	+
Nybacka, S., et al. (2018)	+	-	-	++	X	-
Parker, S. L., et al. (1990)	+	-	X	-	X	-
Patelis, A., et al. (2014)	+	+	X	+	+	++
Patten, S. and Williams, J. (2007)	+	-	X	++	X	+
Puente-Fernandez, C., et al. (2016)	-	-	X	++	X	-
Rentzos, G., et al. (2015)	+	-	X	-	X	-
Rix, K. J., et al. (1984)	+	-	X	++	X	+
Saberi-Firoozi, M., et al. (2007)	-	-	X	-	X	-
Soost, S., et al. (2009)	-	-	X	+	X	-
Tomba, C., et al. (2012)	+	-	++	++	X	+
van Gils, T., et al. (2016)	-	-	X	+	X	-
Vesa, T. H., et al. (1998)	+	-	X	++	X	+
Vierk, K. A., et al. (2007)	-	-	X	++	X	-
Woods, R. K., et al. (2001)	+	-	X	+	X	+
Legend	- Poor	+ Moderate	++ Strong	X N/A		

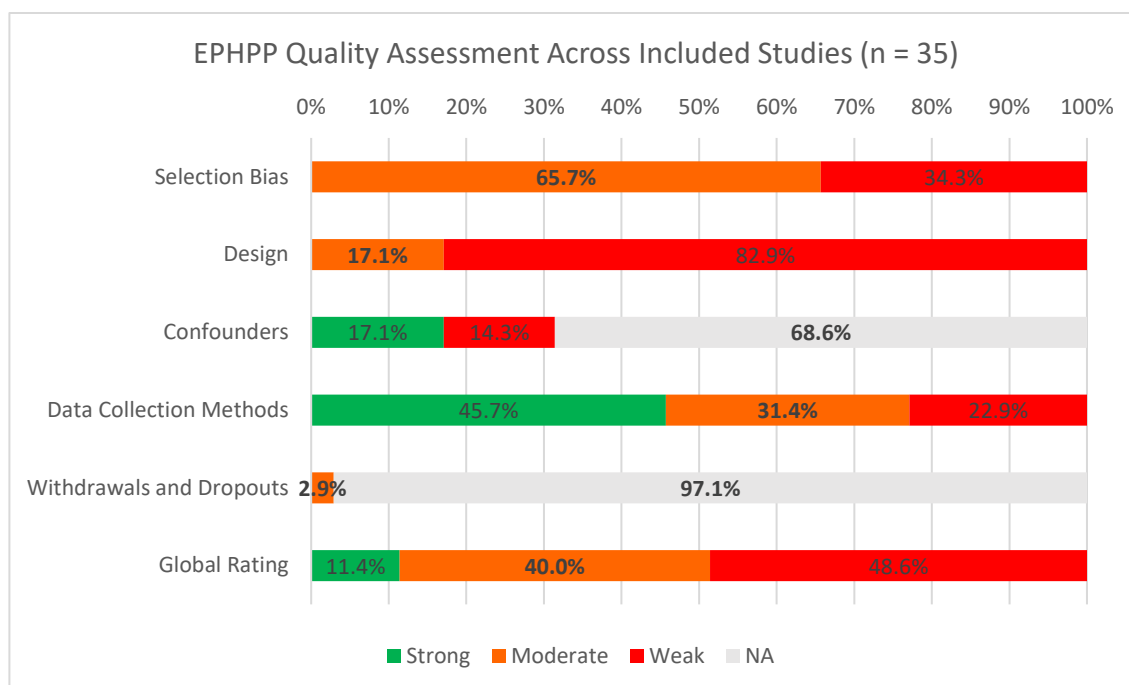


Figure 2. Adapted EPHPP quality assessment rating across studies

3.4 Identification and Measurement of Psychological Variables

Psychological variables were identified and grouped thematically through discussion between A.D., E.G., and L.H. Fifteen variables were identified and were categorised into five groups; (a) Common Mental Disorders (CMD) and Distress: *anxiety; health anxiety; symptom anxiety; depression; psychological distress* in sixteen studies, (b) Personality: *neuroticism, extraversion, psychoticism* in three studies (c) Somatisation: *somatic complaints, symptom severity* in twelve studies, (d) Stress and Coping: *stress, coping* in one study (e) Beliefs and Cognitions: *health-related; food-related; healthcare-related* in five studies. The findings for each variable are discussed below under relevant subheadings and are summarised in detail in Appendix IV.

Psychological correlates were measured using a range of validated self-report measures and diagnostic assessments, which are described in Table 2. The most frequently used self-report measures were the Hospital Anxiety and Depression scale (HADS; n = 5) (Zigmond & Snaith, 1983), the IBS Severity Scoring System (IBS-SSS; n = 5) (Francis, Morris, & Whorwell, 1997), and the Subjective Health Complaints Inventory (SHC; n = 3) (Eriksen, Ihlebæk, & Ursin, 1999). Three studies assessed CMD using

questions relating to medical history in purpose-created questionnaires (Golley et al., 2015; Jakobsen et al., 2016; van Gils et al., 2016). Measures used were primarily self-report, however, five studies (Berstad, Undseth, Lind, & Valeur, 2012; Lillestøl et al., 2010; Manu et al., 1993; Patten & Williams, 2007; Rix et al., 1984) used interviewer-conducted diagnostic instruments including the Mini-International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998), National Institute of Mental Health Diagnostic Interview Schedule (NIMH-DIS) (Robins, Helzer, Croughan, & Ratcliff, 1981), the World Mental Health Composite International Diagnostic Interview (WMH-CIDI) (Kessler & Üstün, 2004), and the Clinical Interview Schedule (CIS) (Goldberg, Cooper, Eastwood, Kedward, & Shepherd, 1970).

3.5 Psychological Correlates

Twenty-two studies investigated psychological correlates of PFI (17/22 cross-sectional and 5/22 case-control), summarised under the five psychological variables, CMD and Distress, Personality, Somatisation, Stress and Coping, and Beliefs and Cognitions. See Table 4 for a plot summary of statistical results at the bivariate and multivariate level, and Appendix V for a summary chart of methodological quality rating of studies which included psychological factors.

3.5.1 Common Mental Disorders and Distress

Sixteen studies investigated CMD and Distress (14/16 cross-sectional, 2/16 case-control) in PFI under five variables; *anxiety* (n = 11; 9/11 cross-sectional, 2/11 case-control), *health anxiety* (n = 2 cross-sectional), *symptom anxiety* (n = 3 cross-sectional), *depression* (n = 12; 10/12 cross-sectional, 2/12 case-control), and *distress* (n = 6; 5/6 cross-sectional, 1/6 case-control).

3.5.1.1 Anxiety

Eleven studies examined anxiety and PFI, using a range of measures to gauge reported anxiety. Six studies used validated self-report measures, four studies used diagnostic interviews to assess the incidence of reported anxiety, and one study relied on medical history. Nine of the studies were cross-sectional, and two were case-control

design, whereby individuals with PFI were compared against a matched control group. Only four studies conducted multivariate analyses, which would allow one to look at contributing factors to PFI. Results were inconsistent. Six studies reported significant findings, and five studies did not determine significantly increased anxiety in PFI (Bohn et al., 2013; Lind, Lied, et al., 2010; Manu et al., 1993; Rix et al., 1984; Tomba, Baldassarri, Coletta, Cesana, & Basilisco, 2012).

Two studies established an increased prevalence of reported anxiety in PFI (Patten & Williams, 2007; van Gils et al., 2016). Patten and Williams (2007) assessed prevalence in the Canadian population using the WMH-CIDI, drawing on a large sample ($n = 36,984$), to establish increased incidence of social phobia in individuals with PFI. However, confidence intervals for respondents with and without PFI overlap, therefore the significance of this finding is mixed. van Gils et al. (2016) determined individuals with PFI were at increased odds of reporting anxiety, however, this community study relied on self-reported medical history. Lillestøl et al. (2010) additionally reported 34% of PFI outpatients met criteria for an anxiety disorder on the MINI, however, the proportion of matched controls who met criteria was not reported, and it is difficult to assess the significance of this finding.

Four studies determined significantly increased anxiety on self-report measures in PFI compared to those without PFI (Dainese et al., 2014; Knibb et al., 1999; Lillestøl et al., 2010; Nybacka et al., 2018), and two additionally found women with PFI reported higher levels of anxiety than men (Knibb et al., 1999; Lillestøl et al., 2010). Of note, mean scores were below clinical cut-off in two of the studies (Lillestøl et al., 2010; Nybacka et al., 2018) and Lillestøl et al. (2010) did not determine group differences in case-level anxiety. Dainese et al. (2014) concluded HADS-anxiety scores were significantly increased and above clinical threshold in PFI-L, however, following logistic regression, significant findings were not retained.

In summary, the evidence is inconsistent. There is some evidence of a higher prevalence of anxiety in PFI, and four studies concluded anxiety was increased compared to controls. Two studies found women with PFI reported higher anxiety than men. The

only study that reported clinically significant levels of anxiety did not retain a significant association between anxiety and PFI-L at multivariate analyses (Dainese et al., 2014).

3.5.1.2 Health Anxiety

Health anxiety refers to a conceptual fear of illness and disease that can contribute to hypervigilance and the misinterpretation of symptoms as an indication of a serious illness (Salkovskis, Rimes, Warwick, & Clark, 2002). Two studies measured health anxiety at a multivariate level.

In a cross-sectional community study from Hungary, Elieson et al. (2017) determined health anxiety was significantly associated with reported PFI, and further determined health anxiety was a significant mediator of reported PFI (Elieson et al., 2017). Of note, the methodological quality of this study was poor; sample characteristics and the level of confounders controlled in analysis or criterion variables set were not adequately described. Conversely, a population-based study from Australia found no association between PFI-G and health anxiety (Golley et al., 2015).

3.5.1.3 Symptom Anxiety

GI symptom-specific anxiety (GSA) has been thought to contribute to distress and symptomatology in IBS patients (Labus, Mayer, Chang, Bolus, & Naliboff, 2007), a patient group that frequently reports PFI. The Visceral Sensitivity Index (VSI) (Labus et al., 2004) is used to measure GSA (Labus et al., 2004). A related construct of somatosensory amplification (SSA) refers to the tendency to be hypervigilant to the experience of somatic sensations and appraise them as aversive (Barsky, Goodson, Lane, & Cleary, 1988).

Three studies explored symptom anxiety. Elieson et al. (2017) concluded SSA was significantly associated with PFI. A cross-sectional study by Lind, Lied, et al. (2010) explored whether symptom anxiety relates to symptom severity that individuals with PFI report. The authors determined higher scores on the VSI were reported by those who scored above threshold on the HADS-A, a measure of general anxiety. Conversely, Bohn et al. (2013) found no significant correlations between GSA and PFI. In summary, the evidence is inconsistent, and the role of symptom anxiety and visceral sensitivity should be further explored.

3.5.1.4 Depression

Twelve studies examined depression and PFI. Seven studies used validated self-report measures, two studies used diagnostic interviews to assess the incidence of depression, and three studies relied on self-reported medical history. Ten studies were cross-sectional, and two were case-control design with a matched control group. Four studies conducted multivariate analyses, and the remainder of the studies reported descriptive and inferential data. Results were inconsistent. Significant findings were reported in seven studies. Five did not report significant findings (Bohn et al., 2013; Lillestøl et al., 2010; Lind, Lied, et al., 2010; Manu et al., 1993; Tomba et al., 2012).

Two population studies determined an increased prevalence of depression in PFI. Patten and Williams (2007) employed a structured psychiatric interview, however, Golley et al. (2015) relied on self-reported medical history, and so diagnoses cannot be confirmed. Two community-based studies reported increased odds of PFI amongst individuals with self-reported depression (Hidese, Nogawa, Saito, & Kunugi, 2019; Jakobsen et al., 2016), and of interest, Hidese et al. (2019) established severity of PFI was associated with depression. Both studies had very large samples (11,876 and 64,316 respectively), however, they were cross-sectional designs and did not account for additional variables that could explain their findings. Three studies determined individuals with PFI self-reported significantly higher levels of depression than those without PFI (Dainese et al., 2014; Knibb et al., 1999; Nybacka et al., 2018), however, this was below clinical threshold and Dainese et al.'s (2014) findings were not retained at multivariate analysis. One study concluded women with PFI reported higher depression than men with PFI and male and female controls (Knibb et al., 1999).

Overall, though significant findings were reported in seven studies, no high-quality studies support a role of depression in PFI. Studies that reported significantly increased scores on measures of self-reported depression were not able to establish this above a normal level, and one study that did determine between-group differences was not able to establish this at a multivariate level. Importantly, Patten and Williams (2007) provided population-based confirmation of an increased prevalence of depression in PFI, though effect sizes were not described. Further high-quality evidence is required.

3.5.1.5 Distress

Psychological distress was included as a variable when outcome measures that provided an overall measure of psychological distress without separating anxiety or depression were used. Six studies explored psychological distress. Five of the studies were cross-sectional, and one was case-control; all studies used validated self-report measures to assess distress. Multivariate analyses were conducted in two studies. Two studies did not report significant findings (Monsbakken et al., 2006; Tomba et al., 2012).

Four studies reported increased distress in PFI (Hidese et al., 2019; Knibb et al., 1999; Lillestøl et al., 2010; Rix et al., 1984), however Lillestøl et al. (2010) finding was significant in women only. Knibb et al. (1999) measured distress as a higher likelihood of meeting psychiatric caseness, and this was additionally found in the female-PFI subgroup. (Knibb et al., 1999; Lillestøl et al., 2010). However, Knibb et al. (1999) note that the percentage of women meeting case-level distress was not more than a reference group comprised of university and NHS staff. Of interest, Hidese et al. (2019) reported that distress increased with PFI severity (increased number of offending foods).

Overall, there is limited evidence indicating increased psychological distress in PFI. Two studies found women report increased distress, and one study found severity of PFI may influence distress, however, further high-quality evidence is needed.

3.5.2 Personality Traits

Three studies, two of which were cross-sectional and one case-control, explored personality traits and PFI, of which one conducted multivariate analysis.

Three studies investigated neuroticism and PFI, of which two reported levels of neuroticism were significantly higher in PFI, in both male and female subgroups (Knibb et al., 1999; Lillestøl et al., 2010), as compared to controls. At a multivariate level, Golley et al. (2015) did not determine any association between neuroticism and PFI. One study measured extraversion and psychoticism, and determined levels of extroversion were found to be significantly higher in women with PFI compared to women without PFI, and compared to men with PFI, and increased levels of psychoticism in men with PFI compared to women with PFI (Knibb et al., 1999).

In summary, it is not possible to conclude personality traits influence PFI. Only one study investigated more than one personality trait, and though reported significant group differences, the methodological quality of this study is poor, and response rate was low. Further, the scores obtained by both the PFI and control groups were not significantly different from a norm group consisting of undergraduates and professionals.

3.5.3 Somatisation

Somatisation includes reported extraintestinal symptoms (pain, stiffness, headache, fatigue) and GI symptoms (bowel changes, gas, bloating, pain, discomfort), and can be measured by the reported frequency of somatic complaints and reported symptom severity in relation to PFI. Thirteen studies investigated somatisation in PFI (9/13 cross-sectional and 4/13 case-control), and ten demonstrated significant findings.

3.5.3.1 *Somatic Complaints*

Somatic complaints were measured by increased frequency of complaints, total number of symptoms reported, or scores on measures of somatisation. Eight studies measured somatic complaints, four were case-control, and four were cross-sectional. Two reported data at the multivariate level.

At a bivariate level, five studies determined individuals with PFI reported more somatic complaints as compared to individuals with chronic fatigue (Manu et al., 1993), controls (Knibb et al., 1999; Lind et al., 2005; Lind, Lillestol, et al., 2010), and increased reporting in women (Knibb et al., 1999; Lind, Lied, et al., 2010). At a multivariate level, two studies demonstrated a significant association between somatic complaints and PFI (Jakobsen et al., 2016; Tomba et al., 2012). One study indicated that women report more GI symptoms than men but did not provide a test statistic (Lind et al., 2008).

Of interest, three studies with PFI samples measured somatic complaints using the Subjective Health Complaints (SHC) inventory (Eriksen et al., 1999), concluding that individuals with PFI reported increased frequency of somatic complaints over a 30-day period than controls (Lind et al., 2005; Lind, Lillestol, et al., 2010), and that women reported more somatic complaints than men (Lind, Lied, et al., 2010). Across these

studies, the most common complaints were bloating, diarrhoea, gas discomfort, stomach pain headache, tiredness, and back pain (Lind et al., 2005; Lind, Lied, et al., 2010; Lind, Lillestol, et al., 2010). In summary, individuals with PFI report more somatic complaints and report them more frequently than those without PFI.

3.5.3.2 Symptom Severity

Nine studies, seven cross-sectional and two case-control, investigated GI and extraintestinal symptom severity in individuals with PFI, of which seven reported significant findings.

Five studies were comprised of IBS samples. At a multivariate level, one determined a significant association between GI symptom severity and PFI-L (Dainese et al., 2014). At a bivariate level, three studies determined that individuals with increased severity of PFI (who reported more offending foods) had increased GI symptom severity (Bohn et al., 2013; Lee et al., 2019; Nybacka et al., 2018) and extraintestinal symptom severity (Bohn et al., 2013). Nybacka et al. (2018) additionally concluded individuals with IBS and PFI report greater extraintestinal symptom severity, but not GI symptom severity, than those with IBS alone. One study did not report significant findings (Monsbakken et al., 2006).

Four studies were comprised of PFI outpatients. Two case-control studies concluded that individuals with PFI report increased GI and extraintestinal symptom severity compared to controls (Lind et al., 2005; Lind, Lillestol, et al., 2010). Two cross-sectional studies were comprised of PFI outpatients only. Lind, Lied, et al. (2010) reported that symptom anxiety was significantly associated with GI symptom severity, but only explained 7% of the variance. The authors additionally concluded women had significantly increased extraintestinal symptom severity than men (Lind, Lied, et al., 2010). One study did not provide a test statistic, though reported 55% of PFI outpatients had severe GI symptoms (Berstad et al., 2012).

Overall, evidence supports increased GI and extraintestinal symptom severity in PFI. Of note, five studies were comprised of IBS samples, and a large proportion of PFI samples met IBS criteria (Berstad et al., 2012; Lind et al., 2005; Lind, Lillestol, et al., 2010).

3.5.4 Stress and Coping

Stress impacts gastrointestinal motility and function and has been reported as a contributing factor in functional gastrointestinal disorders (FGID) (Mayer, 2000; Mayer, Naliboff, Chang, & Coutinho, 2001; Suarez, Mayer, Ehlert, & Nater, 2010). Stress and coping were investigated by one case-control study with PFI outpatients (Lind, Liljestol, et al., 2010). The authors investigated job stress and determined PFI outpatients reported significantly lower job stress than controls. The authors additionally concluded that both groups used similar coping strategies, with no significant group differences. Overall, limited evidence precludes drawing conclusions regarding the contributing effects of perceived stress and coping strategies, and additional high-quality research is required.

3.5.5 Beliefs and Cognitions

Beliefs and cognitions, including those towards health, food and healthcare were investigated in five studies (4/5 cross-sectional and 1/5 case control).

3.5.5.1 *Health Related*

Health-related beliefs were reported by three studies. At a multivariate level, no association between PFI and health worries was found (Elieson et al., 2017), on the Modern Health Worries Scale (Petrie et al., 2001). One study with a female-only sample reported a significant association between PFI and poor perceived health, though this was collected through reported history, and not measured on a standardised assessment (Jakobsen et al., 2016). At a bivariate level, Lind et al. (2005) found no group differences in sum scores of health-related worries between individuals with PFI, controls and the general population.

3.5.5.2 *Food Related*

Food related worries and beliefs were reported in three studies. At a multivariate level, (Elieson et al., 2017) reported no association between food-related worries and PFI. At a bivariate level, Lind et al. (2005) determined PFI outpatients were significantly more worried about food additives and genetically modified food than controls, and Barr (2013) determined fewer of those with PFI-L had positive beliefs about milk products.

3.5.5.3 Healthcare Beliefs

Healthcare beliefs were assessed in two cross-sectional studies, which determined PFI and PFI-G were significantly associated with positive beliefs about complementary and alternative medicine (Elieson et al., 2017; Golley et al., 2015), and less receptiveness towards conventional medicine (Golley et al., 2015).

Overall, research into the role of cognitions and beliefs to PFI is limited, and further evidence exploring PFI-related beliefs is required.

3.6 Clinical Correlates

Twenty-six articles (21/26 cross-sectional, 4/26 case control and 1/26 longitudinal) reported clinical correlates including reported health conditions. The results are described below under relevant subheadings and are summarised in detail in Appendix VI. These were grouped into gastrointestinal (GI) (16 studies; 13/16 cross-sectional, 3/16 case control), atopic (12 studies; 11/12 cross-sectional, 1/12 longitudinal), and long-term conditions (6 studies; 5/6 cross-sectional, 1/6 case control). GI correlates refer to diagnoses of IBS or described family histories. Atopy refers to a genetic or hereditary predisposition to develop allergic disease including allergies, dermatitis and asthma. Long-term conditions refer to chronic fatigue syndrome, rheumatoid arthritis, fibromyalgia and musculoskeletal pain, and other reported conditions. See Table 4 for a plot summary of statistical results at the bivariate and multivariate level, and Appendix VII for a summary chart of methodological quality rating of studies which included clinical factors.

3.6.1.1 Gastrointestinal

Sixteen articles provided evidence of GI correlates of PFI. In five studies with PFI-only samples, 71% - 99% met criteria for IBS (Berstad et al., 2012; Lillestøl et al., 2010; Lind et al., 2005; Lind, Lied, et al., 2010; Lind, Lillestøl, et al., 2010). Five studies recruited individuals with IBS (Bohn et al., 2013; Dainese et al., 2014; Lee et al., 2019; Monsbakken et al., 2006; Nybacka et al., 2018), of which PFI was reported in each study. Two of these studies additionally reported that participants with IBS had a significantly higher prevalence of PFI than controls (Lee et al., 2019; Nybacka et al., 2018).

In community and population-based studies, four concluded reporting PFI increased the odds of IBS (Puente-Fernandez et al., 2016; Saberi-Firoozi et al., 2007; van Gils et al., 2016; Vesa, Seppo, Marteau, Sahi, & Korpela, 1998) at a multivariate level. Additionally, van Gils et al. (2016) determined individuals with PFI-G more often reported a family history of Coeliac Disease. At a bivariate level, two studies reported IBS was significantly more prevalent in PFI-G (Cabrera-Chavez et al., 2017; Golley et al., 2015). In summary, there is strong evidence for gastrointestinal clinical correlates of PFI.

3.6.1.2 Atopy

Twelve studies investigated atopy and PFI. Of note, three studies used previously-defined samples investigating respiratory health (Patelis et al., 2014; Woods et al., 2001), and asthma (Rentzos et al., 2015), and one study used a pre-determined sample of adults with rheumatoid arthritis (Liden et al., 2010).

Four studies with non-clinical samples reported significant findings at multivariate level. Allergy, dermatitis (Gelincik et al., 2008; Puente-Fernandez et al., 2016; Soost et al., 2009), a family history of atopy (Gelincik et al., 2008; Puente-Fernandez et al., 2016), and asthma (Gelincik et al., 2008; Woods et al., 2001) were positive predictors of PFI, and atopy was found to be associated with PFI in a study spanning 15 countries (Woods et al., 2001). Five studies reported bivariate significant findings. Prevalence of PFI was significantly higher in patients with IBS and atopy (Nybacka et al., 2018) and individuals with asthma (Rentzos et al., 2015). Allergies (Jansen et al., 1994; Liden et al., 2010; Patelis et al., 2014); skin-related manifestations (Liden et al., 2010; Patelis et al., 2014); asthma (Patelis et al., 2014; Rentzos et al., 2015); and family history of atopy (Jansen et al., 1994; Puente-Fernandez et al., 2016) were more often reported by those with PFI. Two studies with PFI outpatients did not report a test statistic; 38% reported at least one atopic disease (Berstad et al., 2012), and 30% reported a family history of atopy (Parker, Leznoff, Sussman, Tarlo, & Krondl, 1990). One study did not report significant findings (Dainese et al., 2014). In summary, there is strong evidence for atopic conditions in reported PFI.

3.6.1.3 Long-Term Conditions

Six studies described long-term conditions. Four studies reported comorbidities described by individuals with PFI, and two articles investigated PFI in pre-determined clinical conditions including rheumatoid arthritis (Liden et al., 2010) and chronic fatigue (Manu et al., 1993), with 27% and 13.5% reporting PFI, respectively.

At a multivariate level, in a female-only community sample, Jakobsen et al. (2016) determined that the odds of PFI increased with increasing comorbidities reported. The authors additionally concluded self-reported chronic fatigue, and hypothyroidism, and fibromyalgia were significantly associated with PFI (Jakobsen et al., 2016), yet conversely, van Gils et al. (2016) community sample found no association between these conditions and PFI-G (wheat and/or gluten intolerance). One study did not report a test statistic, though indicated chronic fatigue and fibromyalgia was reported by 85% and 71% of PFI outpatients, respectively (Berstad et al., 2012). Monsbakken et al. (2006) did not report any significant findings. In summary, there is some evidence that individuals with PFI report comorbid long-term conditions. This was self-reported in three studies, with no medical evidence to confirm, and two studies used pre-defined clinical samples and are thus not representative of the general population.

3.7 Psychosocial Correlates

Twenty-four studies reported psychosocial correlates (23/24 cross-sectional and 1/24 case-control, 1/25 longitudinal), including demographic factors of sex, age, and ethnicity, and socioeconomic factors of employment, education, and living. The results are described below and in Table 4, and summarised in detail in Appendix VIII. See Table 4 for a plot summary of statistical results at the bivariate and multivariate level, and Appendix IX for a summary chart of methodological quality rating of studies which included psychosocial factors.

3.7.1.1 Demographic Factors: Sex, Age and Ethnicity

Twenty-one studies explored sex differences and PFI. Fifteen reported significant findings. Across included studies, a large proportion of the samples were female (see Table 2). At a multivariate level, seven studies determined female sex was a predictor of

PFI (Golley et al., 2015; Puente-Fernandez et al., 2016; Saberi-Firoozi et al., 2007; Soost et al., 2009; van Gils et al., 2016; Vesa et al., 1998; Woods et al., 2001). Eight studies reported the prevalence of PFI was significantly higher in females (Barr, 2013; Cabrera-Chavez et al., 2017; Golley et al., 2015; Hidese et al., 2019; Jansen et al., 1994; Patelis et al., 2014; Puente-Fernandez et al., 2016; Vierk et al., 2007), and one study found women reported more symptomatic foods than men (Bohn et al., 2013). One study described significant findings but did not describe these further (Elieson et al., 2017). Six studies did not report significant findings (Dainese et al., 2014; Gelincik et al., 2008; Lee et al., 2019; Monsbakken et al., 2006; Rix et al., 1984; Tomba et al., 2012).

Nineteen cross-sectional studies explored age and PFI, eight of which determined age was a significant correlate of PFI. At a multivariate level, two studies reported younger age was a positive predictor of PFI (Gelincik et al., 2008; Jakobsen et al., 2016). At a bivariate level, four studies reported younger age was more common in PFI (Barr, 2013; Hidese et al., 2019; Soost et al., 2009; van Gils et al., 2016). However, Soost et al. (2009) did not report significance levels. Contrarily, Parker et al. (1990) reported PFI was associated with older age. One study reported significant findings but did not describe these further (Elieson et al., 2017). Eleven studies did not report significant findings (Bohn et al., 2013; Cabrera-Chavez et al., 2017; Dainese et al., 2014; Jansen et al., 1994; Lee et al., 2019; Monsbakken et al., 2006; Rix et al., 1984; Saberi-Firoozi et al., 2007; Vesa et al., 1998; Vierk et al., 2007; Woods et al., 2001).

Two cross-sectional studies included information regarding ethnicity. Barr (2013) found a higher proportion of non-Caucasians reported PFI-L, and Vierk et al. (2007) reported no findings.

Overall, there is strong evidence for an association between PFI and female sex. There is some evidence that PFI is associated with a younger age, however, further exploration is required.

3.7.1.2 Socioeconomic Factors: Employment, Education and Living Circumstances

Six studies explored employment and PFI, and three reported significant findings. Not being in full-time employment was significantly associated with PFI in a female-only sample (Jakobsen et al., 2016), and Lind, Lillestol, et al. (2010) determined part-time

employed PFI outpatients reported more health complaints than matched-controls without PFI. Rix et al. (1984) reported a larger proportion of PFI outpatients were more likely employed in 'professional' careers. Three studies reported no significant findings (Jansen et al., 1994; Lee et al., 2019; Parker, Krondl, & Coleman, 1993).

Seven studies investigated education, and three studies reported significant findings. A higher level of education was more often reported in those with PFI (Vierk et al., 2007), significantly associated with PFI (Jakobsen et al., 2016; Soost et al., 2009), and approached significance in one study (van Gils et al., 2016). Three studies did not report findings (Jansen et al., 1994; Lee et al., 2019; Parker et al., 1993).

Three cross-sectional studies explored living circumstances with significant findings. Jakobsen et al. (2016) determined that not living with a partner, poor childhood economic living conditions, and living in an urban region predicted PFI. van Gils et al. (2016) additionally determined living in an urban region predicted PFI-G. Woods et al. (2001) study spanning 15 countries determined that living in Germany, Iceland, Sweden and Norway were all significant predictors of PFI.

In summary, there is some evidence that a higher level of education is associated with PFI, and that not being in full-time employment is reported by some with PFI. Evidence surrounding living conditions and living in an urban region is limited and may be an area of interest in future research.

Table 4. Summary of Statistical Findings

Number of studies reporting significant findings (refer to Table 1 for reference numbers)													
		Cross-Sectional				Case-Control				Longitudinal			
		Descriptive/Bivariate		Multivariate		Descriptive/Bivariate		Multivariate		Descriptive/Bivariate		Multivariate	
		<i>p</i> < 0.05	NS / *	<i>p</i> < 0.05	NS/*	<i>p</i> < 0.05	NS/*	<i>p</i> < 0.05	NS/*	<i>p</i> < 0.05	NS/ *	<i>p</i> < 0.05	NS/*
Psychological Correlates	CMD and Distress	Anxiety (n = 11)	5 ^{25,32,5,12, 22}	4 ^{3,18,28, 31}	1 ⁵	1 ¹⁵	1 ²⁰						
		Health Anx. (n = 2)		1 ⁶	1 ⁸								
		Symp. Anx. (n = 3)		1 ³	2 ^{6,18}								
		Depression (n = 12)	5 ^{8,25,5,12,22}	3 ^{3, 18,31}	2 ^{9,10}		2 ^{15,20}						
		Distress (n = 6)	2 ^{12,28}	2 ^{21, 31}	1 ⁹	1 ¹⁵							
	Personality	Neuroticism (n = 3)	1 ¹²	1 ⁸		1 ¹⁵							
		Extraversion (n = 1)	1 ¹²										
		Psychoticism (n = 1)	1 ¹²										
	Somat-isation	Somatic Comp. (n = 8)	2 ^{12,18}		2 ^{10,31}	3 ^{16,19,20}	1 ¹⁷						
		Symptom Severity (n = 9)	5 ^{18,5,3,13,22}	2 ^{2*,21}		2 ^{16, 19}							
Clinical Correlates	Stress & Coping	Stress (n = 1)					1 ¹⁹						
		Coping (n = 1)					1 ¹⁹						
	Beliefs & Cognitions	Health & Illness (n = 3)			1 ¹⁰	1 ¹⁶							
		Food (n = 3)	1 ¹		1 ⁶	1 ¹⁶							
		Healthcare (n = 2)			2 ^{6,8}								
Clinical Correlates	GI (n = 16)	9 ^{4,8,13,22,3} 5, 21,2,18		4 ^{26,29,32} ,33		3 ^{15,16,19}							
	Atopy (n = 12)	5 ^{22,27,11,14,26}	3 ^{5, 2*, 23*}	4 ^{35,26,7,} 30						1 ²⁴			
	Long-Term Conditions (n = 6)	2 ^{10,32}	1 ^{2*,} 14**,21**	1 ¹⁰		1 ^{21*}							

		Cross-Sectional				Case-Control				Longitudinal			
		Descriptive/Bivariate		Multivariate		Descriptive/Bivariate		Multivariate		Descriptive/Bivariate		Multivariate	
		<i>p</i> < 0.05	NS / *	<i>p</i> < 0.05	NS/*	<i>p</i> < 0.05	NS/*	<i>p</i> < 0.05	NS/*	<i>p</i> < 0.05	NS / *	<i>p</i> < 0.05	NS/*
Psychosocial Correlates	Demo-graphic												
	Sex (<i>n</i> = 21)	9 ^{1,3,4,8,9,11,26,34}	6 ^{5,7,13,21,28,31}	7 ^{8,26,29,30,32,33,35}						1 ²⁴			
	Age (<i>n</i> = 19)	5 ^{1,9,32,23,6}	12 ^{3,4,5,11,13,21,28,29,33,34,35,30*}	2 ^{7,10}									
	Socio-economic												
	Ethnicity (<i>n</i> = 2)	1 ¹	1 ³⁴										
	Employment (<i>n</i> = 6)	1 ²⁸	3 ^{11,13,23}	1 ¹⁰	1 ¹⁹								
	Education (<i>n</i> = 7)	1 ³⁴	4 ^{11,13,23,32+}	2 ^{10,30}									
	Living Circumstances (<i>n</i> = 4)			1 ^{10,32,35}									

Legend: *p* < 0.05 = significant at the .05 level, NS = not significant, * = no test statistic used so cannot determine significance

Reference numbering refers to numbering described in Table 1

Note: Anxiety and Depression; Ref. 5 had significant findings at bivariate level and no significant findings at multivariate level

** Long-term conditions; Refs 14** & 21** 100% of samples had Rheumatoid Arthritis and Chronic Fatigue respectively

+ Education Level; Ref 32+ approached statistical significance

4 Discussion

4.1 Summary of Findings

The purpose of the current systematic review was to evaluate the literature for evidence of psychological, clinical and psychosocial factors that may be associated with reported PFI. Thirty-five studies that met inclusion criteria and described psychological (n = 22), clinical (n = 26), and psychosocial (n = 24) correlates of PFI were reviewed. Psychological correlates included fifteen psychological variables summarised under five groups; CMD and distress, personality, somatisation, stress and coping, and beliefs and cognitions. Clinical correlates were summarised under gastrointestinal, atopic and long-term conditions. Psychosocial correlates were summarised under demographic and socioeconomic categories.

Prevalence of PFI was reported by up to 9.5% in population studies, up to 51.2% in community studies, and up to 84% in clinical samples. Evidence consistently indicates PFI is more often reported in women as compared to men, and that PFI is associated with frequent reporting of GI and extraintestinal symptoms. Evidence found individuals with PFI often concurrently report GI and atopic conditions. Some evidence suggested increased levels of common mental disorders (CMD) and distress, though data were inconsistent, and often reported at a cross-sectional bivariate level, precluding causal inferences. Findings regarding age were mixed and sociodemographic data were infrequently collected.

4.1.1 Summary of Findings: Psychological Correlates

The evidence supports a significant association between somatisation and PFI. These individuals are more likely to report GI and extraintestinal complaints including bloating, headache, diarrhea, gas, discomfort and tiredness, and increased symptom severity as compared to controls and clinical samples. This suggests that common reactions experienced by those with PFI is consistent with symptoms described in non-allergic food hypersensitivity.

There is some evidence that individuals with PFI self-report elevated anxiety, depression, and distress compared to those without PFI, however, this was predominantly at a descriptive level by comparing mean scores on self-report measures. Exploring this further, it was evident that most of these scores fell below what would be considered clinical threshold, suggesting that case-level distress may not be a significant correlate of PFI. However, studies that measured affect only did so at one time-point, so it is not possible to know the direction of this relationship, if affect fluctuates over time, and what factors are important in contributing to affect. This demonstrates the need for future high-quality research using multivariate analyses and exploring affect at different time points to better understand its role in PFI. Further, prospective research would help identify if affect, thoughts or beliefs are associated with the onset of PFI, as this has not been established

Findings relating to personality traits, stress and coping, and beliefs and cognitions were limited, as these variables were only explored in a small number of studies of poor and moderate quality, and it is difficult to draw conclusions regarding the importance of these factors in PFI. Research in PFI has not yet explored the specific beliefs or illness perceptions that individuals may hold about PFI, and further research should explore worries related to GI sensations (GSA). This would be of interest, as illness perceptions and GSA have been evidenced to contribute to distress IBS (Chilcot & Moss-Morris, 2013; De Gucht, 2015; Knowles et al., 2017; Labus et al., 2004; Labus et al., 2007; Mayer & Raybould, 1990; Rutter & Rutter, 2002), and have been demonstrated as a mechanism of change and improved outcome in psychological interventions for individuals with IBS (Chilcot & Moss-Morris, 2013; Garland et al., 2012; Wolitzky-Taylor, Craske, Labus, Mayer, & Naliboff, 2012).

Few of the studies were methodologically strong. The strongest studies had a case-control design whereby outpatients were compared with matched controls, reducing confounding variables in analyses. However, results do not support causal inferences, without which it is not possible to identify modifiable targets to address in intervention. Further some factors explored including job stress, modern health worries

and CAM-related beliefs are infrequently assessed in the literature and were not measured in a way that allowed for directionality to be understood. Personality, specifically neuroticism, is a widely measured construct in relation to health-behaviours, but its specificity has been critiqued, and it has been suggested that it is most useful as a marker of risk of psychopathology (Ormel et al., 2013; Ormel, Rosmalen, & Farmer, 2004). The results from included studies were generally inconsistent, of poor methodological quality, and study designs employed do not allow causal inferences to be drawn. Further, results do not provide evidence of specific modifiable targets to address in intervention. If future work should wish to identify contributing factors that can be targeted in intervention, high-quality research is needed using multivariate analyses and conducted across multiple time points. Future research should explore factors that have been demonstrated to be important in IBS, including GSA and illness perceptions, as IBS and PFI have considerable characteristic overlap.

4.1.2 Summary of Findings: Clinical Correlates

Evidence demonstrates a strong relationship between IBS and PFI, possibly alluding to shared mechanisms in PFI and IBS. However, it is also possible that individuals with IBS may be more likely to attribute symptoms to PFI, or that GI symptom overlap between these two conditions mean that many individuals with PFI meet criteria for IBS. Evidence from multiple population-based studies demonstrated individuals with PFI reported comorbid atopic conditions including rhinitis, dermatitis/eczema and asthma. Scant evidence supports an increased prevalence of PFI in comorbid long-term conditions. The evidence does not support a better understanding of the relationship between clinical comorbidities and PFI, and whether this is related to stress, immune functioning, neuroendocrine pathways, or other additional mechanisms. Only four studies received a global rating of strong, and all studies were subject to selection bias, including self-selection and purposive sampling methods. High-quality evidence elucidating the role of clinical comorbidities in PFI is required to understand if specific health comorbidities contribute to reporting PFI, or vice versa, and if so, the mechanism of this relationship. This is necessary in order to identify groups that are more likely to experience PFI, and potential targets for a biopsychosocial intervention.

4.1.3 Summary of Findings: Psychosocial Correlates

The results provide consistent evidence for an increased prevalence of PFI in women. This finding is of interest, as there is a higher reported prevalence of IBS in women (Lovell & Ford, 2012a, 2012b; Sperber et al., 2017), demonstrating further similarities between these two conditions. However, this only demonstrates incidence of reporting IBS and PFI, and in light of shortcomings with current evidence, it is not possible to conclude if these represent similar yet separate conditions that women more often report, if PFI is a manifestation of IBS, or if IBS mediates PFI. Research in PFI has not rigorously examined mechanisms posited to underlie IBS, though this could be done in the future with a sample of adults with PFI-only, IBS-only, PFI+IBS, and controls.

Some studies demonstrated an association between PFI and younger age; a higher level of education; and living in an urban region, though evidence was limited. Only one study explored early living conditions and demonstrated a relationship between poor childhood economic conditions and PFI. Early adverse experiences are an established correlate of IBS (Videlock et al., 2009). There are characteristic similarities between PFI and IBS, though drawing conclusions about any further likeness between these conditions is not yet supported by high-quality research. It is possible that early adverse experiences may be a factor associated with PFI, though prospective research is required.

A significant proportion of studies were methodologically moderate and poor, and the only study to receive a global rating of strong was a longitudinal study that only reported on sex differences as a psychosocial correlate. The results indicate psychosocial factors are infrequently measured and high-quality research is needed in order to better understand psychosocial correlates of PFI, as this can help to provide a better understanding of common factors in PFI, and can identify potential factors that may be associated with risk of reporting PFI

4.2 Implications for Future Research and Clinical Practice

The findings of the current review provide evidence that further high-quality research with individuals with PFI is necessary. To better understand factors involved in predictive risk and maintenance of PFI, prodromal, prospective and longitudinal research

in individuals both with and without PFI at baseline is needed. It would be important to assess the presence of IBS and other existing conditions (to separate data for individuals with IBS and other conditions to reduce confounding effects), and measure psychological factors known to contribute to IBS including perceived stress, GSA and illness perceptions, and a defined set of psychosocial predictors that have been demonstrated to contribute to the aetiology and maintenance of IBS including early adverse events and life stressors (Videlock et al., 2009; White et al., 2010; Whitehead et al., 2002).

High-quality evidence of correlates that perpetuate PFI can inform a biopsychosocial model and future psychological interventions to address modifiable factors that influence illness and symptom attributions, unhelpful behaviours such as avoidance, increased vigilance towards visceral sensations, and perceived stress and related distress. The aim would be to improve outcome and QoL for the individual and to help to manage symptoms and the related thoughts and emotions experienced in the context of PFI, as these may contribute to avoidance behaviours. Furthermore, if individuals feel better able to manage PFI and its sequelae, this may contribute to fewer visits to healthcare providers, reduced economic burden, and potentially increased self-efficacy, which is integral to self-management of health conditions (Pimm & Weinman, 1998; Schwarzer & Fuchs, 1996). An intervention could include components of psychoeducation, as well as both cognitive and behaviour-based strategies, which have been implicated in successful interventions in IBS (Chilcot & Moss-Morris, 2013; Garland et al., 2012; Hunt, Moshier, & Milonova, 2009; Wolitzky-Taylor et al., 2012). Further, promoting awareness of the various contributors and correlates of PFI may help inform a physician's response to food intolerance in primary care and may shape the language used to describe reasons for why an individual can experience such distressing symptoms. Skepticism about the existence of PFI can contribute to practitioners' perceptions of patients (Nelson & Ogden, 2008), and differing perceptions about the severity and impact of the condition between medical professionals and individuals with FGID have been reported (Dalton, Drossman, Hathaway, & Bangdiwala, 2004). Communication and the doctor-patient relationship have implications for health-related behaviours and outcome

(Oates, Weston, & Jordan, 2000; Stewart et al., 1999). In IBS, communication has been demonstrated to contribute to the patients experience (Halpert & Godena, 2011), and the doctor-patient relationship contributes to an individual's understanding of their IBS, which is associated with improved QoL and acceptance (Hulme, Chilcot, & Smith, 2018), and may influence the experience of PFI and related outcome. This has not been explored in PFI but might be an important consideration in understanding factors that may contribute to outcome.

4.3 Strengths and Limitations

Significant effort was made to improve the reliability of the current review. The author, in addition to a second and third reviewer, screened the titles and abstracts of all studies, and assessed relevant full text of articles against inclusion and exclusion criteria. Further, data extraction and quality assessment of all included studies was conducted independently by the author, and the second and third reviewer, to reduce bias and enhance rigor. Methodological quality was assessed with an adapted EPHPP, however, a tool designed for cross-sectional studies may have been more appropriate given the significant proportion of cross-sectional studies included in the review. However, quality assessment tools for cross-sectional studies provide an appraisal only, such as the AXIS tool (Downes, Brennan, Williams, & Dean, 2016), without an overall rating of study quality. Further, the Newcastle-Ottawa Scale (NOS) (Wells et al., 2015) has been adapted for use in cross-sectional studies, however a recently published review assessing the AXIS and NOS demonstrated poor to moderate reliability for these tools (Moskalewicz & Oremus, 2019). It is possible that the use of either the AXIS or NOS may have contributed to a stronger quality appraisal, but this might not have reflected evident methodological issues described in the included papers. Finally, findings clearly demonstrate the need for data beyond what cross-sectional studies provide and exploring PFI across multiple time points would provide a more accurate representation of factors associated with PFI.

The results of the current review are limited by the quality of included studies, which were largely moderate and poor. Only one study included data collected at multiple time points. Most studies conducted bivariate analyses, which does not allow for

conclusions to be drawn regarding the nature or direction of correlates of PFI. Only a small number of psychological variables apart from CMD and distress have been investigated, and these were not studied in a way that advances a potential model of PFI, or related evidence. There is no high-quality research studying factors that are hypothesised contribute to IBS including illness perceptions, perceived stress, or GSA. Further, factors evidenced in influencing the onset of IBS including gut infection and early life events have not been fully explored in PFI, and given some reported similarities between IBS and PFI, it is possible that there are aetiological factors important in PFI that have already been established in IBS. Only one study was retrieved in the search exploring PFI following a giardiasis outbreak (Litleskare et al., 2015), however, it did not meet age inclusion criteria, as individuals under the age of 18 were included and data were not separated. Though most studies reported sex and age characteristics, ethnicity and socioeconomic data were rarely collected, therefore it is difficult to understand their role in PFI. Finally, additional factors that contribute to adverse food reactions not accounted for in this review may influence PFI, such as food aversions or food poisoning.

4.4 Conclusions

This is the first systematic review in PFI to the authors' knowledge, and provides an overview of psychological, clinical and psychosocial correlates reported in PFI. Prevalence of PFI was reported by up to 9.5% in population studies, up to 51.2% in community studies, and up to 84% in clinical samples. The findings suggest PFI is associated with female sex, and that those with PFI report more frequent and severe GI and extraintestinal symptoms than those without PFI. There is some cross-sectional evidence that CMD and distress are increased in PFI, though not at clinical threshold, and generally not of high-quality. The findings of the current review indicate similarities with IBS, which should be explored further. These findings have implications for further research which will allow for a better understanding of PFI and may inform future psychological models and therapies.

5 References

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6 Appendices

Appendix I: PRISMA Checklist

Section/topic	#	Checklist item	Reported page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title page
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5-7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	B
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this	7

		information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10 + Figure 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	11 + Table 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 3 + Appendices
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Results section + Appendices
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Figure 2
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18 -
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	39-40
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

Appendix II: Search Strategy

MEDLINE

1. food intolerance.mp. or exp Food Hypersensitivity/ or exp Food Intolerance/
2. (food hypersensitivit* or food sensitivit*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
3. 1 or 2
4. (perceived or self-report* or self report* or subjective).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
5. 3 and 4

PsycINFO

1. (food intolerance or food hypersensitivit* or food sensitivit*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]

EMBASE

1. (food intolerance or food hypersensitivit* or food sensitivit*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
2. nutritional intolerance.mp. or exp nutritional intolerance/
3. 1 or 2
4. (perceived or self-report* or self report* or subjective).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
5. 3 and 4

Global Health

1. (food intolerance or food hypersensitivit* or food sensitivit*).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
2. (perceived or self-report* or self report* or subjective).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]
3. 1 and 2

Web of Science

TI=(food intolerance* OR food sensitivit* OR food hypersensitivit*) AND TI=(perceived OR subjective OR self-report*)

Scopus

(TITLE-ABS-KEY (food AND intolerance OR food AND hypersensitivit* OR food AND sensitivit*) AND TITLE-ABS-KEY (perceived OR self-report* OR self AND report* OR subjective)

Appendix III: Adapted EPHPP

Adapted EPHPP, modified for suitability for cross-sectional and case-control studies with no intervention.

A) Selection Bias

Q1- Are the individuals selected to participate in the study likely to be representative of the target population?

1. Very likely
2. Somewhat likely
3. Not likely
4. Can't tell

Q2 – What percentage of selected individuals agreed to participate?

1. 80 – 100% agreement
2. 60 – 79% agreement
3. Less than 60% agreement
4. Not applicable
5. Can't tell

Rate this section	Strong	Moderate	Weak
<i>See dictionary</i>	1	2	3

B) Study Design

1. Randomised controlled trial
2. Controlled clinical trial
3. Cohort analytic (two group pre +post)
4. Case-control
5. Cohort (one group pre + post)
6. Interrupted time series
7. Other (specify)
8. Can't tell

Rate this section	Strong	Moderate	Weak
<i>See dictionary</i>	1	2	3

C) Confounders

Q1 – Were there important differences between groups?

1. Yes
2. No
3. Can't tell

The following are examples of confounders; race, sex, marital status/family, age, SES (income or class), education, health status

Q2 – If yes, indicate the percentage of relevant confounders that were controlled either in the design or analysis

1. 80-90%
2. 60-79%
3. Less than 60%
4. Can't tell

Rate this section	Strong	Moderate	Weak
<i>See dictionary</i>	1	2	3

D) Data Collection Method

Q1 – Were data collection tools shown to be valid?

1. Yes
2. No
3. Can't tell

Q2- Were data collection tools shown to be reliable?

1. Yes
2. No
3. Can't tell

Rate this section	Strong	Moderate	Weak
<i>See dictionary</i>	1	2	3

E) Withdrawals and Drop Outs

Q1 - For longitudinal studies, were withdrawals and drop-outs in terms of numbers and/or reasons?

1. Yes
2. No
3. Can't tell
4. Not applicable (one-time survey)

Q2 – Indicate the percentage of participants completing the study

1. 80-90%
2. 60-79%
3. Less than 60%
4. Can't tell
4. Not applicable

Rate this section	Strong	Moderate	Weak
<i>See dictionary</i>	1	2	3

Global Rating

- 1 Strong (no weak ratings)**
- 2 Moderate (one weak rating)**
- 3 Weak (two or more weak ratings)**

Appendix IV: Psychological correlates summary of findings

Author (year)	Variable (Measure)	CMD and Distress Findings
Bohn, L., et al. (2013)	Anxiety (HADS) Depression (HADS) Symptom anxiety (VSI)	Anxiety: PFI (as defined as food-related GI symptoms) not significantly correlated with anxiety ($r = -0.11$; $p = 0.13$) Depression: PFI (as defined as food-related GI symptoms) not significantly correlated with depression ($r = -0.05$; $p = 0.50$) Symptom Anxiety: No significant correlations between food-related GI symptoms and symptom specific anxiety ($r = 0.04$; $p = 0.55$)
Dainese, R., et al. (2014)	Anxiety (HADS) Depression (BDI)	Anxiety: PFI-L had higher median HADS-A scores ($Mdn = 13$ [IQR = 8–14] vs. $Mdn = 8$ [IQR = 5–12], $p < 0.01$). No significant association found (OR = 1.270, $p = 0.29$). Depression: PFI-L (vs. non) had higher median BDI scores ($Mdn = 8$ [IQR = 5–10] vs. $Mdn = 3$ [IQR = 2–7], $p < 0.01$). No association found (OR = 1.138, $p = 0.32$).
Elieson, L.M., et al. (2017)	Health anxiety (SHAI) Symptom anxiety (SSAS)	Health Anxiety: PFI associated with health anxiety (OR = 1.103, $p < 0.001$), and health anxiety is a significant mediator of PFI ($b = 1.002$, $p < 0.001$). PFI (vs non-PFI) had higher SHAI scores ($M = 33.98$ (SD = 5.521) vs. $M = 29.79$ (SD = 7.812)), no p value. Symptom Anxiety: PFI associated with somatosensory amplification (OR = 1.041, $p = 0.028$). Following mediation analysis, mediated by health anxiety ($b = -0.0040 \pm 0.214$, NS). PFI ($M = 28.05$, SD = 6.768) had higher mean SSAS scores than non-PFI ($M = 25.71$, SD = 6.307), no p value.
Golley, S., et al. (2015)	Health Anxiety (WI) Depression (Medical History)	Health Anxiety: No significant associations (OR = 1.18; 95% CI [0.88-1.58], $p = 0.26$). Depression: PFI-G (vs. non-PFI-G) more likely to report history of depression (32.9% vs. 19.5%, $\chi^2 (1) = 8.47$, $p < 0.004$).
Hidese, S., et al. (2019)	Depression (Self report) Distress (K6)	Depression: PFI significant and positive predictor for a self-reported lifetime history of clinical depression (OR = 1.46, 95% CI [1.13–1.88], $p = 0.0037$). Individuals with 2 (OR = 1.75), 3 (OR = 2.02), and 4 (OR = 2.27) allergens were significantly more common in the depression group ($p < 0.001$). Distress: PFI (vs non-PFI) associated with severe psychological distress (K6 ≥ 13) (OR = 1.32, $p < 0.001$).
Jakobsen, M.D., et al. (2016)	Depression (Medical History)	Depression: PFI associated with self-reporting depression (OR = 1.30, $p < 0.001$)

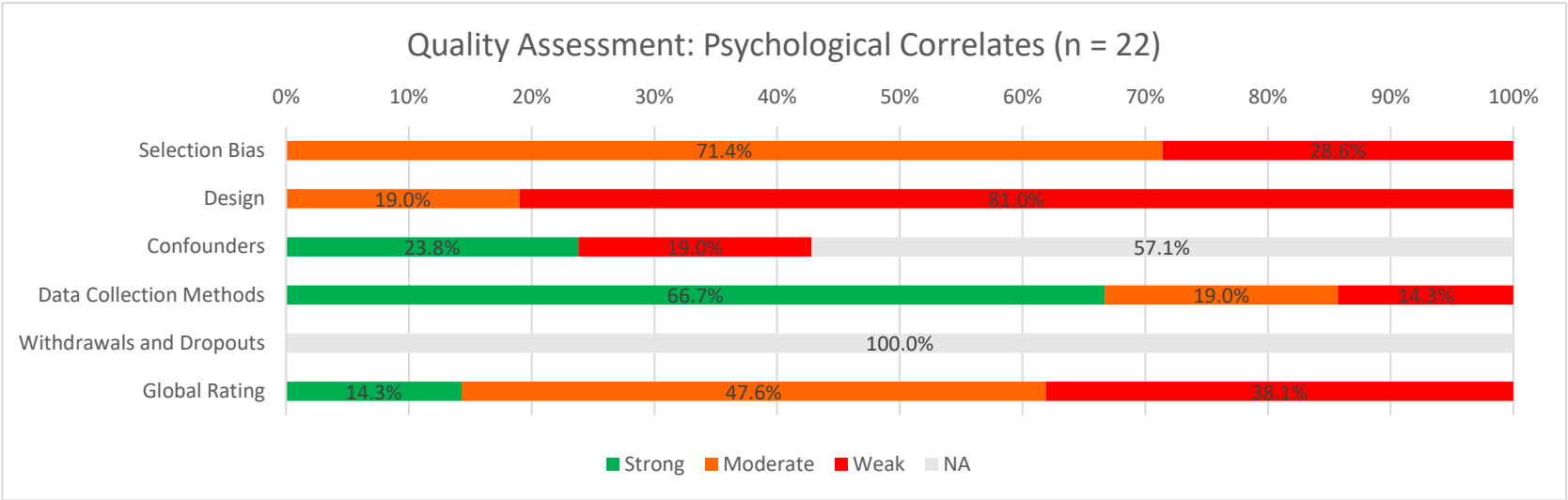
Knibb, R. C., et al. (1999)	Anxiety Depression Distress (all GHQ-28)	Anxiety: Higher scores in PFI sample $t(533)=3.1, p < 0.002$, PFI women vs. non-PFI women, ($t(116)=3.2, p < 0.002$), and PFI women vs. PFI men ($t(134)=3.3, p < 0.001$). Depression: Higher scores in all PFI ($t(187)=52.53, p < 0.01$), PFI women vs. non-PFI women, ($t(106)=2.6, p < 0.02$), and PFI women vs. PFI men ($t(136)=2.1, p < 0.04$). Distress: PFI associated with “at-risk for diagnosis of minor psychiatric disorder”, $\chi^2(3)=8.7, p < 0.03$. PFI women (vs. PFI men) scored significantly higher for psychiatric caseness, $t(136)=2.40, p < 0.02$.
Lillestol, K., et al. (2010)	Anxiety (MINI, HADS) Depression (MINI, HADS, MADRS) Distress (GHQ-30, MINI)	Anxiety: 34.2% PFI met anxiety disorder criteria on MINI (most frequently, GAD and panic disorder). PFI women scored significantly higher than controls on HADS-A ($M = 5.3, SD = 3.7$ vs. $M = 4.0, SD = 3.3, p = 0.013$) and HAD-Total ($p = 0.021$). Case-level HADS-A (≥ 8) found in 23.5% of PFI vs. 12.5% controls ($p > 0.05$; NS). Depression: 15.8% PFI met depressive disorder criteria on MINI; lower prevalence in MADRS findings (8%). No significant difference in HADS-D scores ($M = 2.6, SD = 2.3$ vs. $M = 2.1, SD = 3.0, p = 0.168$). Case-level HADS-D in 2.5% PFI vs. 8.3% (NS). Distress: 56.6% PFI met psychiatric disorder criteria on MINI. PFI associated with higher GHQ-30 scores ($p = 0.022$) in women only.
Lind, R., Lied, G, et al. (2010)	Anxiety (HADS) Depression (HADS) Symptom anxiety (VSI)	Anxiety: Mean HADS-A score ($M = 4.9, SD = 3.5$). Case-level HADS-A (≥ 8) found in 24%. Gender or symptom severity (SHC & IBS-SQ) not associated. Depression: Mean HADS-D score ($M = 4.6, SD = 2.4$). Case-level HADS-D (≥ 8) found in 14%. Gender or symptom severity (SHC & IBS-SQ) not associated. Symptom Anxiety: Symptom anxiety and HAD-A significantly correlated ($r = 0.48, p < 0.0001$). Higher VSI scores found in individuals with HADS-A score ≥ 8 ($p = 0.0004$), and IBS-SQ score ≥ 25 ($p = 0.001$). Symptom anxiety was a significant predictor of GI symptom severity (IBS-SQ) ($\beta = 0.186; p = 0.02$).
Manu, P., et al. (1993)	Anxiety Depression (both NIMH-DIS)	Anxiety: Anxiety disorder prevalence similar between groups (11.1% vs. 14.8%). Depression: Prevalence of depressive disorders similar between groups (66.6% vs. 62.9%). No significant differences in depressive complaints between groups (NS).
Monsbakken, K. W., et al. (2006)	Distress (HSCL-10)	Distress: No significant differences in HSCL-10 scores between PFI ($M = 1.61, SD = 0.55$) and non-PFI ($M = 1.52, SD = 0.30$), $p = 0.35$. No significant correlation between PFI and distress ($r_s = 0.04, p = 0.73$).
Nybacka, S., et al. (2018)	Anxiety Depression (both HADS)	Anxiety: PFI scored significantly higher than non-PFI ($M = 9.2$ vs $7.5, p = 0.029$). Depression: PFI scored significantly higher than non-PFI ($M = 5.6$ vs $4.5, p = 0.049$).
Patten, S. & Williams, J. (2007)	Anxiety (WMH-CIDI) Depression (WMH-CIDI)	Anxiety: Significant differences in social phobia prevalence [95% CI] in adults >45 with PFI (3.5% [2.3-4.7]) vs. non-PFI (1.8% [1.5-2.2]), $p < 0.05$. Of entire social phobia group (all ages) 14.5% [9.7-19.4] were PFI adults $>45, p < 0.05$. Panic disorder NS. Depression: Significant differences in MDD prevalence [95% CI] in adults >45 with PFI (5.7% [4.2-7.2]) vs. non-PFI (3.0% [2.6-3.4]), $p < 0.05$. Of entire MDD group (all ages), 14.5% [10.8-18.2] were adults >45 with PFI, $p < 0.05$.

Rix, K.J., et al. (1984)	Anxiety (CIS) Distress (CIS, SRT)	Anxiety: Psychiatry outpatients had higher mean scores on CIS anxiety ($M = 2.05$ vs. $M = 1.89$, no SD) and anxious manifest abnormalities ($M = 0.17$ vs. $M = 0.9$, no SD) than PFI outpatients ($p < 0.05$) Distress: Mean CIS scores for PFI ($M = 20.5$, Range:10-36) significantly higher than dFA ($M = 5$, Range: 2-8), $p < 0.01$, but not significantly different than psychiatry outpatients ($M = 21.4$, no SD), $p > 0.05$. No significant findings on SRT; psychological changes were not induced by food in PFI outpatients. No significant differences on psychiatric diagnosis, personal/family history of psychiatric disorder, or number who had seen a psychiatrist.
Tomba, C., et al. (2012)	Anxiety Depression Distress (all SCL-90R)	Anxiety: PFI-L did not have significantly higher anxiety t scores, ($p > 0.05$; NS). Depression: PFI-L did not have significantly higher depression t scores, ($p > 0.05$; NS). Distress: PFI-L did not have significantly higher global severity index (distress) t scores, ($p > 0.05$; NS). <i>Note no $M(SD)$ reported for any of the above.</i>
van Gils, T., et al. (2016)	Anxiety (Medical History)	Anxiety: 16.3% of PFI-G reported anxiety vs 3.1% non-PFI-G (OR = 6.0, 95% CI [2.5-14.3], $p < 0.001$)
Author (year)	Variable (Measure)	Personality Findings
Golley, S., et al. (2015)	Neuroticism (NEO-N)	PFI-G not associated with neuroticism (OR = 0.82; 95% CI [0.55-1.21], $p = 0.31$).
Knibb, R. C., et al. (1999)	Neuroticism Extroversion Psychoticism (all EPQ)	Neuroticism: Higher scores in all PFI ($t(516) = 4.25$, $p < 0.0001$), PFI women vs non-PFI women, ($t(283) = 3.5$, $p < 0.001$), and PFI men vs non-PFI men, ($t(231) = 2.44$, $p < 0.02$), indicating more neurotic. Extroversion: Higher scores in PFI women vs. non-PFI women, ($t(283) = 2.1$, $p < 0.04$), and vs. PFI men, ($t(129) = 2.67$, $p < 0.008$), indicating more extroverted. Psychoticism: Higher scores in PFI men vs. PFI women, ($t(101) = 2.74$, $p < 0.007$), indicating less socially compliant. Scores increased with an increase in social deprivation ($r = 0.18$, $p < 0.04$) in PFI.
Lillestol, K., et al. (2010)	Neuroticism (EPQ-N)	PFI ($M = 9.2$, $SD = 5.2$) had significantly higher scores than controls ($M = 6.5$, $SD = 5.5$) $p < 0.001$. This was found in male as well as in female subgroups (scores not reported).
Author (year)	Variable (Measure)	Somatisation Findings
Berstad, A., et al. (2012)	Symptom severity (IBS-SSS)	Severe IBS symptoms (55%).

Bohn, L., et al. (2013)	Symptom severity (Non-GI: PHQ-15 GI: IBS-SSS)	Degree of PFI associated with increasing IBS symptom severity ($p = 0.004$) and increasing extraintestinal symptom severity ($p = 0.030$), such that IBS patients who reported a higher number of food items causing GI symptoms had increased symptom severity.
Dainese, R., et al. (2014)	Symptom severity (IBS-SSS)	IBS patients with PFI-L had higher symptom severity scores [305 (192–326) vs. 233 (129–304) $p = 0.05$]. PFI-L was significantly associated with IBS symptom severity (OR = 1.019, 95% CI [1.002–1.037], $p = 0.02$)
Knibb, R. C., et al. (1999)	Somatic complaints (GHQ-28)	PFI (vs. non-PFI) reported significantly more somatic symptoms, ($t(533) = 3.1$, $p < 0.002$). Also found in PFI-women vs non-PFI women ($t(293) = 3.24$, $p < 0.001$), and PFI-women vs. PFI men ($t(136) = 2.5$, $p < 0.01$).
Lee, H.J., et al. (2019) χ^2 , Fisher's exact	Symptom severity (GI: IBS-SSS)	Patients who reported a higher number of food items causing GI symptoms had increased IBS symptom severity ($p = 0.020$)
Lind, R., et al. (2005)	Somatic complaints (SHC) Symptom severity (SHC)	Somatic Complaints: PFI reported more complaints ($Mdn = 22.5$, IQR = 15.5 – 32) vs. healthy controls ($Mdn = 5$ IQR = 2 – 9) & general population ($Mdn = 9.5$, IQR = 4 – 15.5), $p < 0.0001$. Five most common complaints were tiredness, bloating, headache, diarrhoea, & back pain. 39% of PFI reported ≥ 15 complaints in last 30 days. Symptom Severity: PFI had higher SHC severity scores, $p < 0.001$ (for all five domains: GI, Musculoskeletal, pseudoneurology, allergy, flu). 65% of PFI (vs. 14% general population) scored above normal (≥ 20).
Lind, R., et al. (2008)	Somatic complaints (no measure)	Somatic Complaints: Concluded that results demonstrate that more women than men report GI symptoms. No test statistic or additional data provided.
Lind, R., Lied. G, et al. (2010)	Somatic complaints (SHC) Symptom severity (Non-GI: SHC GI: IBS-SQ)	Somatic Complaints: Women, had more complaints each month vs men ($p = 0.03$). Five most common complaints were tiredness, gas discomfort, stomach pain, headache, and diarrhoea. 47% reported ≥ 15 complaints in last 30 days. Symptom Severity: Women ($M = 14.7$, $SD = 5.5$) had higher SHC severity scores than men ($M = 11.2$, $SD = 6.8$), $p = 0.03$. IBS symptom severity similar in men and women. Symptom anxiety significant predictor for GI symptom severity ($\beta = 0.186$, $p = 0.02$).
Lind, Lillestol, K., et al (2010)	Somatic complaints (SHC) Symptom severity (SHC)	Somatic Complaints: PFI ($M = 23.5$, $SD = 9.7$) reported significantly more total subjective health complaints than controls ($M = 11.7$, $SD = 9.8$), $p = 0.0001$. The five most common complaints were gas discomfort, diarrhoea, stomach discomfort, tiredness and headache. 36% of PFI reported ≥ 15 complaints in last 30 days. Symptom Severity: PFI had higher SHC severity scores on GI, $p < 0.001$; allergy ($p < 0.001$), pseudoneurology ($p < 0.05$) and musculoskeletal complaints ($p = 0.002$). 67% of PFI (vs 17% controls) scored above normal (≥ 20).
Manu, P., et al. (1993)	Somatic complaints (NIMH-DIS)	PFI (vs. non-PFI) had more lifetime functional extraintestinal symptoms ($p < 0.05$), including irregular menstrual periods ($\chi^2 = 6.1$, $df = 1$, $p < 0.02$), dizziness/light headedness ($\chi^2 = 4.1$, $df = 1$, $p < 0.05$), and diarrhoea ($\chi^2 = 4$, $df = 1$, $p < 0.05$). PFI had significantly higher (33% vs. 7%) prevalence of somatisation disorder ($p < 0.025$).
Monsbakken, K. W., et al. (2006)	Symptom Severity (Musculoskeletal Questionnaire)	Musculoskeletal pain score not significantly different between PFI and non-PFI ($p = 0.13$, NS). However, there were significant correlations between musculoskeletal pain score and psychological distress (HSCL-10) ($r_s = 0.43$, $p < 0.001$).

Nybacka, S., et al. (2018)	Symptom severity (Non-GI: PHQ-15, GI: IBS-SSS)	IBS with PFI patients ($M = 12.9$, no SD) reported more extraintestinal symptoms than non-PFI ($M = 10.8$, no SD) $p = 0.023$. No differences in IBS symptom severity found.
Tomba, C., et al. (2012)	Somatic complaints (SCL-90R)	High somatisation t scores associated with PFI-L (OR = 4.184; 95% CI [1.704–10.309], $p = 0.0009$).
Author (year)	Variable (Measure)	Stress & Coping Findings
Lind, Lillestol, K., et al (2010)	Stress (CJSQ) Coping (UCL)	Stress: PFI (vs. controls) reported lower job stress ($p = 0.01$) and perceived less stress according to communication ($p = 0.02$), leadership ($p = 0.04$), and relocation ($p = 0.01$). No 'workload' group differences. Coping: PFI and controls used similar coping strategies with no significant differences in total scores ($M = 42.7$, 95% CI (41.2–44.) vs. $M = 42.9$, 95% CI (41.6–44.2). PFI generally used an active coping pattern, scoring high on instrumental mastery-oriented coping and low on avoidance coping.
Author (year)	Variable (Measure)	Beliefs & Cognitions Findings
Barr, S.I., (2013)	Food Related (MHBS)	PFI-L (vs. non-PFI-L) had lower MHBS scores ($M = 25.1(\pm SE) 0.3$ vs. $29.3(\pm 0.1)$, $F=158$, $p < 0.001$), indicating fewer of those with PFI-L responded in a manner indicating positive beliefs about milk products.
Elieson, L. M., et al. (2017)	Health (MHW) Food Related (MHW) Healthcare (HCAMQ)	Health Worries: PFI ($M = 71.05$, $SD = 24.807$) higher MHW mean scores than non-PFI ($M = 66.10$, $SD = 18.993$), no p value reported. No significant association for health worries (OR = 1.001, $p = 0.817$) Food Worries: PFI ($M = 17.31$ $SD = 5.941$) had higher Tainted Food subscale scores than non-PFI ($M = 15.13$, $SD = 5.213$). No significant association between PFI and food worries (OR = 1.035, $p = 0.123$) Healthcare Beliefs: PFI associated with positive complementary and alternative medicine attitudes (OR = 0.932, $p < 0.001$).
Golley, S., et al. (2015)	Healthcare (History)	CAM: PFI-G significantly associated with positive receptiveness to complementary medicine (OR = 1.68, 95% CI [1.32-2.14], $p < 0.001$), and less receptiveness to conventional medicine (OR = -0.50; 95% CI [0.49-0.76], $p < 0.001$).
Jakobsen, M.D., et al. (2016)	Health (Medical History)	PFI is associated with poor perceived health (OR = 2.56, $p < 0.001$)
Lind, R., et al. (2005)	Health (MHW) Food Related (MHW)	Health Worries: Sum scores on the MHW did not differ significantly between PFI ($Mdn = 66.5$, IQR[46-85.5]) versus controls ($Mdn = 61.5$, IQR[44-75.5]) or general population ($Mdn = 57$, $SD = 43-74$), $p > 0.05$. PFI were significantly more worried about overuse of antibiotics ($p < 0.001$), amalgam in dental fillings ($p < 0.01$). Food Worries: PFI significantly more worried about food additives ($p < 0.05$), and genetically modified food ($P < 0.05$).

Appendix V: EPHPP Quality Assessment Across Studies Included in ‘Psychological Correlates’



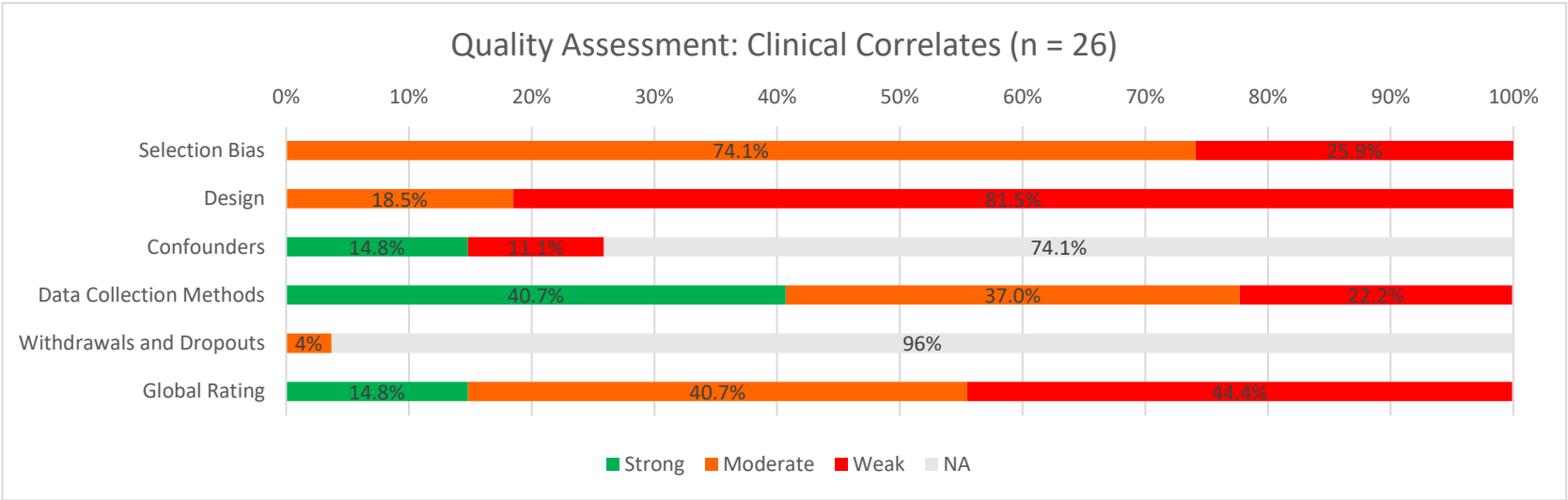
Appendix VI: Clinical correlates summary of findings

Author (year)	Long-Term Conditions	Gastrointestinal	Atopy		
			Allergy	Skin-Related	Asthma
Berstad, A., et al. (2012)	Fibromyalgia (71%) Chronic fatigue (81%)	99% met IBS criteria	≥1 atopic disease (38%)		
Bohn, L., et al. (2013)		100% had IBS			
Cabrera-Chavez, F., et al. (2017)		IBS (14.3% vs. 4.7%, $p < 0.001$)			
Dainese, R., et al. (2014)		100% had IBS.	<i>Atopic disease and family history atopy NS</i>		
Gelincik, A., et al. (2008)			Nasal allergy (OR = 1.56, 95% CI [1.27-1.78], $p < 0.001$) Familial atopy (OR = 4.28, 95% CI [3.58-4.88], $p < 0.001$)	Dermatitis (OR = 3.88, 95% CI [3.29 4.48], $p < 0.001$)	OR = 1.45, 95% CI [1.18-1.78], $p < 0.001$
Golley, S., et al. (2015)		IBS (21.2% vs 8.7%, $p < 0.001$).	Food allergy ($p < 0.001$).		
Jakobsen, M. D., et al. (2016)	Muscle pain (OR = 1.80, $p < 0.001$) Fibromyalgia (OR = 1.72, $p < 0.001$) Back pain (OR = 1.24, $p < 0.001$) Hypothyroidism (OR = 1.61, $p < 0.001$) Chronic fatigue (OR = 2.55, $p < 0.001$) Odds of PFI increase with increasing number of concurrent comorbidities. 2 concurrent comorbidities (OR = 1.16, $p < 0.001$), 3 concurrent comorbidities (OR = 3.02, $p < 0.001$), 4 concurrent comorbidities (OR = 4.12, $p < 0.001$), 5 or 6 concurrent comorbidities (OR = 4.82, $p < 0.001$).				
Jansen, J. J. N., et al. (1994)			Other allergies ($p < 0.001$) Familial allergies ($p < 0.0001$)		
Lee, H. J., et al. (2019)		IBS Sample PFI+ IBS 79.2% vs. PFI in Control 44.8% $p < 0.001$			

Liden, M., et al. (2010)	100% had rheumatoid arthritis		Allergy ($p < 0.001$) childhood food allergy ($p < 0.05$)	Eczema $p < 0.05$	
Author (year)	Long-Term Conditions	Gastrointestinal	Allergy	Atopy Skin-related	Asthma
Lillestol, K., et al. (2010)		88.5% met IBS criteria			
Lind, R., et al. (2005)		71% met IBS criteria 18% dyspepsia			
Lind, R., Lied, G. et al. (2010)		94% met IBS criteria			
Lind, R., Lillestol, K. et al. (2010)		76.5% met IBS criteria			
Manu, P., et al. (1993)	100% had chronic fatigue. <i>Severity or duration of fatigue (NS).</i>				
Monsbakken, K. W., et al. (2006)	<i>State of health, fibromyalgia, musculoskeletal pain syndrome, musculoskeletal pain score (NS)</i>	100% IBS <i>h.pylori, abdominal symptom score (NS)</i>			
Nybacka, S., et al. (2018)		100% IBS PFI in IBS 19% vs. PFI in Control 6% $p = 0.025$	PFI & Atopic IBS prev. (28% vs. 9% $p = 0.002$).		
Parker, S. L., et al. (1990)			30% reported family history of food allergy.		
Patelis, A., et al. (2014)			Rhinitis ($p < 0.001$) IgE aeroallergens sensitisation ($p < 0.001$).	Eczema $p < 0.001$	$p = 0.001$ Further, 13-18% of sample had asthma.
Puente-Fernandez, C., et al. (2016)		Gastritis (OR = 4.26 95% CI [3.28-5.53], $p < 0.001$)	Allergic disease (OR = 2.09, 95% CI [1.03-4.24], $p = 0.04$) Allergic rhinitis (OR = 2.01, 95% CI [1.46-2.78], $p < 0.001$) Maternal ($p = 0.003$) and Parental ($p = 0.02$) history food allergy	Dermatitis (OR = 2.48, 95% CI [1.55-3.96], $p < 0.001$) Maternal history atopic dermatitis ($p = 0.03$) Parental history urticaria ($p = 0.03$)	
Rentzos, G., et al. (2015)					PFI prevalence: 53.1% vs.29.8%, p

			< 0.001. Further, 38.2% asthmatics.	
Saberi-Firoozi, M., et al. (2007)		IBS (OR = 1.47, 95% CI [1.09-1.98], $p = 0.011$)		
Soost, S., et al. (2009)		Allergic rhinitis (OR = 1.38; 95% CI (1.14-1.67) $p < 0.01$) in women only Eczema (OR = 2.33; 95% CI (1.78–3.06), $p < 0.01$) in women only		
van Gils, T., et al. (2016)	Anaemia (OR = 3 95% CI [1.3-6.8], $p = 0.01$) Chronic headache (OR = 4.1 95% CI [1.6-10.6], $p < 0.01$)	37% of PFI-G reported IBS (OR = 5.9 95% CI [3.1-11.1], $p < 0.001$) Family: Coeliac disease (OR= 3.4, 95% CI [1.4-10.5], $p < 0.05$)		
Vesa, T. H., et al. (1998)		IBS (OR = 4.6, [2.1-10.1])		
Woods, R. K., et al. (2001)		Atopy OR =1.38, 95% CI [1.23-1.55] Wheeze in past 12 months (OR = 1.37, 95% CI [1.16-1.60]), Asthma history (OR = 1.71, 95% CI [1.09-2.66]) Current asthma medication (OR = 1.44, 95% CI [1.21-1.70]) all at $p < 0.05$.		

Appendix VII: EPHPP Quality Assessment Across Studies Included in ‘Clinical Correlates’

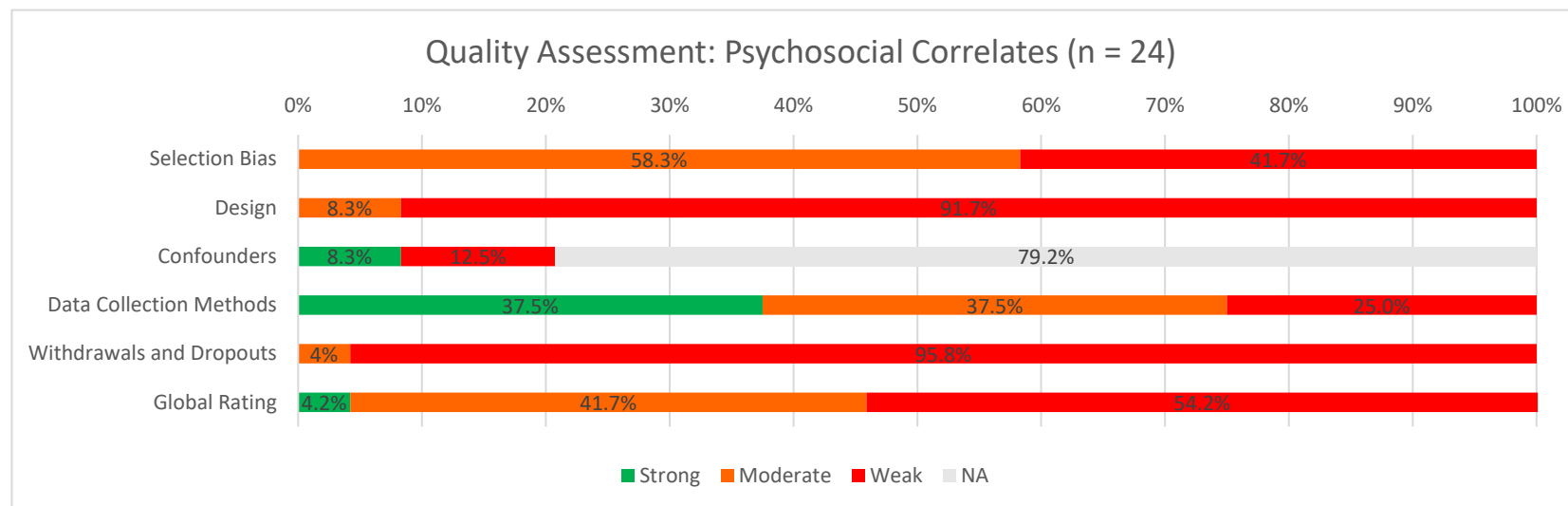


Appendix VIII: Psychosocial correlates summary of findings

Author (year)	Sex	Age	Ethnicity	Socioeconomic
Barr, S. I. (2013)	PFI-L prevalence higher in females (20% vs. 12.3%, $p < 0.001$)	Younger Age (18.3% vs 13.3%, $p = 0.005$)	Not white (26% v. 15.4%, $p = 0.002$)	
Bohn, L., et al. (2013)	Females reported more food items ($p = 0.06$).	NS		
Cabrera-Chavez, F., et al. (2017)	PFI-G prevalence higher in females (4.1% vs. 1.6%, $p < 0.001$).	NS		
Dainese, R., et al. (2014)	NS	NS		
Elieson, L. M., et al. (2017)	Significant, but not further described, $p < 0.001$	Significant, but not further described, $p < 0.001$		
Gelincik, A., et al. (2008)	NS	Younger age (OR = 1.32, 95% CI [1.19-1.49], $p = 0.03$)		
Golley, S., et al. (2015)	PFI-G prevalence higher in females (11% vs. 3%, $p < 0.001$), PFI predicted by female sex (OR = 0.26, 95% CI [0.14-0.46], $p < 0.001$)			
Hidese, S., et al. (2019)	PFI associated with female sex ($p < 0.001$)	Younger age ($p < 0.001$).		
Jakobsen, M. D., et al. (2016)	<i>Sample all female</i>	Younger age (OR = 0.97, $p < 0.001$)		Living in urban region (OR = 1.10, $p = 0.003$) >9 years of education (OR = 1.69, $p < 0.001$) Not in full-time work (OR = 1.3, $p < 0.001$) Poor childhood conditions (OR = 1.2, $p < 0.001$)
Jansen, J. J. N., et al. (1994)	PFI prevalence higher in female sex (15% vs. 9%, $p < 0.005$).	NS		Education, occupational group (NS)

Lee, H. J., et al. (2019)	NS	NS	Education, employment, (NS)
Lind, R., Lillestol, K. et al. (2010)			Part-time employed > health complaints ($p = 0.0005$).
Monsbakken, K. W., et al. (2006)	NS	NS	
Parker, S. L., et al. (1990)		Older age ($p < 0.05$)	Education, marital status, employment status (NS).
Patelis, A., et al. (2014)	PFI prevalence higher in female sex (61.6% $p < 0.001$)		
Puente-Fernandez, C., et al. (2016)	PFI prevalence higher in female (37.5% vs 19.8%), $p < 0.001$. PFI predicted by female sex (OR = 2.43, 95% CI [1.86-3.18], $p < 0.001$).		
Rix, K. J., et al. (1984)	NS	NS	PFI more likely 'professionals' ($p < 0.05$)
Saberi-Firoozi, M., et al. (2007)	PFI-L predicted by female sex (OR = 1.29, 95% CI [1.05-1.59], $p = 0.015$).	NS	
Soost, S., et al. (2009)	PFI predicted by female sex (OR = 1.83, 95% CI [1.39–2.39] $p < 0.001$)	Younger age (no p reported)	Higher education (OR = 1.92, [1.19–2.85], $p < 0.001$).
Tomba, C., et al. (2012)	NS		
van Gils, T., et al. (2016)	PFI-G predicted by female sex (OR = 2.8, 95% CI [1.4–5.7], $p < 0.01$)	Younger age ($p = 0.001$)	Living in urban region (OR = 2.5 95% CI [1.3–4.8], $p < 0.01$). <i>Trend higher education</i>
Vesa, T. H., et al. (1998)	PFI-L predicted by female sex (OR = 2.1, 95% CI [1.1 - 4.0])	NS	
Vierk, K. A., et al. (2007)	PFI prevalence higher in female sex (11.4% vs 6.5%, $p < 0.001$).	NS	NS Higher education (11.3% vs 6.6% high school >, $p < 0.001$).
Woods, R. K., et al. (2001)	PFI predicted by female sex (OR = 1.47, 95% CI [1.24-1.74], $p < 0.05$)	NS	Living in Iceland, Norway, Sweden, Germany (OR = 1.72, 2.00, 1.98, 1.76 respectively) all $p < 0.05$.

Appendix IX: EPHPP Quality Assessment Across Studies Included in 'Psychosocial Correlates'



CHAPTER 2

EMPIRICAL PROJECT

UNDERSTANDING THE ROLE OF PSYCHOLOGICAL
FACTORS IN INDIVIDUALS WITH PERCEIVED FOOD
INTOLERANCE: AN EXPLORATORY STUDY

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Supervised by Dr Emma Godfrey and Dr Lyndsay Hughes

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Abstract

BACKGROUND: Reproducible adverse food reactions are a defining feature of food hypersensitivity (FH). Perceived food intolerance (PFI) is a poorly understood nonimmune FH reported by up to 35% of individuals and characterised by diagnostic challenges. PFI is associated with psychological distress, gastrointestinal (GI) and extraintestinal symptoms, food avoidance, poor quality of life (QoL) and repeated healthcare visits. However, limited research has explored a role of psychological factors in PFI and related distress.

AIM: The present longitudinal study aimed to investigate illness perceptions, coping strategies and additional factors including perceived stress, symptom severity, functional impairment and PFI severity on outcome in PFI, including reported negative affect (anxiety and distress) and food-related QoL (FR-QoL).

METHODS: Adults over the age of 18 who reported PFI were recruited through convenience sampling via advertisements on social media and King's College London research recruiting and invited to participate in an online study. A purpose-built questionnaire was developed and administered using the Qualtrics platform at three time points including baseline (T1), 3-month follow up (T2), and 6-month follow up (T3). Study aims and hypotheses were assessed using bivariate and multivariate analyses with baseline data, and mediation analyses were conducted using longitudinal data.

RESULTS: There were no significant changes in scores on outcome measures across time points, and average anxiety scores were above clinical cut off, indicative of elevated self-reported anxiety in this population. Baseline cross-sectional results indicated that the strongest contributors to negative affect were extraintestinal symptom severity, emotional representations of PFI, and coping responses of self-blame and disengagement. The strongest contributors to poor FR-QoL were illness representations including illness identity and emotional representations, perceived stress, GI symptom severity and PFI severity. Across all measured outcomes, a coping response of positive reframing improved outcome. Longitudinal mediation analyses demonstrated coping responses of self-blame and disengagement had significant complete and partial mediating effects on illness perceptions in anxiety and distress, whereas illness perceptions had significant complete and partial mediating effects in FR-QoL. Symptom severity of extraintestinal and GI symptoms, additionally contributed to poor outcome.

CONCLUSIONS: Evidence suggests that outcome in PFI may be maintained by modifiable factors including illness representations and coping responses, and by cognitive, emotional, and behavioural reactions to somatic symptoms and additional consequences of PFI. A psychological intervention to improve outcome based on an Acceptance and Commitment Therapy (ACT) framework is proposed.

1 Introduction

1.1 Background

The term ‘adverse food reactions’ is often used to describe negative reactions to food, which could be the result of toxins, food poisoning, taste aversion, or hypersensitivity reactions (Ortolani & Pastorello, 2006; Teufel et al., 2007). A European Academy of Allergy and Clinical Immunology (EAACI) position statement recommends when a reaction “causes objectively reproducible symptoms and signs, initiated by exposure to a defined stimulus at a dose tolerated by normal subjects” (p.816), in the context of food, the term food hypersensitivity (FH) should be used (Johansson et al., 2001), which includes both allergic hypersensitivity (immune-mediated) and nonallergic hypersensitivity (nonimmune mediated). For the purpose of this paper, allergic hypersensitivity, which produces immediate reactions that often occur within minutes of exposure to the offending food, will be referred to as ‘food allergy’ (FA). Non-immune nonallergic hypersensitivity, which is associated with delayed reactions that occur hours to days after exposure to the offending food, has been referred to in position statements as ‘nonallergic food hypersensitivity’ (Johansson et al., 2001) and ‘food intolerance’ (Boyce et al., 2011), and in the current paper will be referred to as ‘perceived food intolerance’ (PFI). The term ‘food hypersensitivity’ (FH) will be used as an umbrella term when referring to both FA and PFI.

The term PFI was selected as an overarching term to reflect all forms of nonimmune food intolerance including those that are undefined and those that are more well understood such as lactose, fructose, and biogenic amine intolerances. The pathophysiology of the GI symptoms caused by lactose and fructose sugars is understood, however, many intolerances are subjectively experienced but difficult to investigate and diagnose due to lack of definable pathology and characteristic delayed onset, including, but not limited to, intolerances to food additives and sulphites (Ortolani & Pastorello, 2006; Skypala, 2011). Furthermore, the current dissertation relied on self-reported intolerance and did not verify nor test reproducibility in the sample, hence it is difficult to confirm if it would meet the criterion definition of ‘hypersensitivity’ (Johansson et al.,

2001). Finally, 'intolerance' is a more widely recognised and used term by lay persons and the media (Dreborg, 2015; Reese et al., 2017). The experiences, reactions and symptoms that individuals with PFI have are very real, and it is hoped that this explanation for chosen terminology does not reflect otherwise.

A large proportion of individuals report PFI in the absence of a verified FA, which contributes to diagnostic challenges for medical practitioners (Nelson & Ogden, 2008), repeated healthcare visits and increased economic burden (Fox et al., 2013; Hazeldine, Worth, Levy, & Sheikh, 2010; Jones & Burks, 2017). Fox et al., (2013) concluded that adults with self-reported FH visit health professionals an average of 11.17 times per year with an overall mean cost of care of \$2016 (international dollars), compared to 7.11 visits per year and mean costs of \$1089 for controls. Further, consequences of PFI extend to personal and social domains, and individuals with PFI report increased distress, food restriction and avoidance, worries about the perceptions of others, and limitations on social activities and travel, which can all contribute to poorer quality of life (QoL) (Arslan, Lind, Olafsson, Florvaag, & Berstad, 2004; Biesiekierski, Newnham, Shepherd, Muir, & Gibson, 2014; Knibb, Armstrong, et al., 1999; Knibb et al., 2000; Nettleton, Woods, Burrows, & Kerr, 2010; Schiefert & Matteucci, 2018).

1.1.1 Diagnosis

Accurate diagnosis of FH requires documented clinical history and evidence of exclusion of other factors and diagnoses that could account for adverse food reactions (e.g. Inflammatory Bowel Disease; IBD), however, relying on self-reported history alone may lead to over-reporting (Rona et al., 2007) or inconsistent accounts (Knibb, Booth, et al., 1999). This is a significant consideration as unless FH is confirmed, epidemiological data may not be representative of the true prevalence and incidence of FH. Alongside a clinical history, evidence of immune involvement is needed to diagnose FA, and a positive oral food challenge is necessary to clinically confirm FH reactions (Renz et al., 2018).

FA pathology can be demonstrated by an often-immediate immunological response seen from skin prick tests, which are often used as a first-line tool in allergy clinics and in research due to their relative ease of administration. However, skin prick test

methodology is not standardised and findings alone are not sufficient to diagnose FA (Muraro et al., 2014; Renz et al., 2018). The gold standard diagnostic method is the double-blind placebo-controlled food challenge (DBPCFC) (Muraro et al., 2014), which can verify both FA and PFI reactions, however, it is not often offered as a first-line diagnostic method as it is time-consuming, laborious and expensive (Muraro et al., 2014).

In PFI, a lack of definable immunological pathology and the delayed nature of PFI reactions have led to diagnostic challenges that affect medical practitioners and those with PFI alike. Hydrogen breath tests have been used to test for lactose and fructose intolerances, however, some research has implied these tests are often unreliable and may have limited clinical value (Bratten, Spanier, & Jones, 2008; Yao & Tuck, 2017; Yao et al., 2017). A DBPCFC can be used to verify undefined PFI, though often is not due to cost and time requirements, and without a positive DBPCFC, diagnosis is less clear. More recently, complementary and alternative medicine (CAM) practitioners, pharmacies and direct-to-consumer companies have offered food intolerance testing such as IgG antibody tests, hair analysis, antigen leucocyte cellular antibody test and applied kinesiology to offer PFI diagnoses, though these are consistently reported to not have clinical validity and are not recommended (Sicherer & Sampson, 2018; Stapel et al., 2008; Teuber & Porch-Curren, 2003). However, as a result of diagnostic challenges individuals with PFI experience, they may be more likely to seek alternative explanations and evidence for their symptoms (Lomer, 2015). Some evidence suggests individuals with PFI report that they are more receptive to CAM (Elieson, Domotor, & Koteles, 2017; Golley, Corsini, Topping, Morell, & Mohr, 2015), and less receptive to conventional medicine (Golley et al., 2015), however, this was not explored in a way to measurably understand how this translates to the use of conventional medicine versus CAM, though research from the United States indicated 22% of individuals with FA had undergone CAM diagnostic assessments (Ko, Lee, Muñoz-Furlong, Li, & Sicherer, 2006).

1.1.2 Prevalence and Epidemiology

There is a large discrepancy between the reported prevalence of PFI and FA. A meta-analysis including 51 papers conducted by Rona et al. (2007) concluded that up to

35% of the general population report PFI, and a recent systematic review (see Chapter 1) determined that prevalence of PFI was reported by up to 9.5% in population studies, up to 51.2% in community samples, and up to 84% in clinical samples (including IBS, chronic fatigue and rheumatoid arthritis samples). However, epidemiological studies consistently demonstrate that only 0.9 – 3% of adults have verified FA (Muraro et al., 2014; Nwaru et al., 2014; Rona et al., 2007; Woods, Abramson, Bailey, & Walters, 2001; Woods et al., 2002; Zuberbier et al., 2004). A systematic review by Nwaru et al. (2014) reported a pooled lifetime prevalence of self-reported FH of 17.3%, yet only a 2.7% prevalence confirmed through immunological markers, and 0.9% prevalence confirmed from a positive food challenge.

It has proven difficult to get an accurate estimate of the prevalence of FH because of the lack of an affordable and consistently reproducible diagnostic test. The DBPCFC is considered gold standard, but is a costly and time consuming procedure and not widely used (Muraro et al., 2014; Ortolani & Pastorello, 2006; Rona et al., 2007; Sicherer & Sampson, 2014; Skypala, 2011). Of interest, most prevalence studies in FH use diagnostic tools that demonstrate immune sensitisation. This can help evidence FA but may lead to inconsistencies in the true prevalence of PFI, as PFI is not immune mediated. However, the data from research that has used a food challenge suggests that ‘hypersensitivity’ (Johansson et al., 2001) criteria is difficult to meet in PFI, as it appears a large portion of PFI reactions are not objectively reproducible, considering the discrepancy in prevalence’s reported in Nwaru et al.’s (2014) study. True estimates of the prevalence of PFI are difficult to know, though previous research has established that PFI is more often reported by women (see Chapter 1).

1.1.3 Common Reactions and Offending Foods

There is currently no cure for FA; patients must eliminate the offending food and receive substantial education about how to avoid the offending food. In FA, IgE reactions are associated with rapid-onset symptoms ranging from itching, burning, tingling and swelling in the mouth and/or throat, to the life-threatening reaction of anaphylactic shock (Muraro et al., 2014; Ortolani & Pastorello, 2006; Skypala, 2011). A US population-based

survey reported the most commonly reported foods in FA are shellfish, milk, peanut, tree nut and fin fish (Gupta et al., 2019), and a European systematic review reported that cow's milk, egg, peanut, tree nuts, fish, and shellfish were most often reported as trigger foods in FA (Nwaru et al., 2014).

PFI symptoms are both intestinal (symptoms within the GI system; GI distress, bloating, abnormal bowel movements) and extraintestinal (symptoms outside of the GI system; fatigue, headaches, musculoskeletal pain, and skin reactions) (Kelsay, 2003; Ortolani & Pastorello, 2006; Sicherer & Sampson, 2014; Zopf, Baenkler, Silbermann, Hahn, & Raithel, 2009). A recent systematic review (see Chapter 1) concluded the most commonly reported GI symptoms included GI bloating, flatulence, abdominal discomfort, abdominal pain, nausea, constipation and diarrhea, and extraintestinal symptoms included tiredness, headache, joint and/or muscle pain, mood changes and/or irritability. Common offending foods in PFI have rarely been robustly measured, though results of a systematic review (see Chapter 1) determined that foods most often self-reported as causing symptoms were wheat, gluten, dairy (including milk and cheese), fruits, vegetables (including legumes and cruciferous vegetables), and eggs. However, offending foods and substances in PFI can also include foods containing vasoactive amines (e.g. histamine), salicylates, caffeine, food additives and sulphites (Ortolani & Pastorello, 2006; Reese et al., 2017; Skypala, 2011; Zopf et al., 2009).

1.2 Biological Factors Associated with PFI

1.2.1 Immunological Factors

PFI reactions are not specifically immune-mediated. Immune mediation is characteristic of FA through food-specific immunological antibodies (predominantly IgE) and cellular mechanisms following ingestion, airborne inhalation or skin contact to the food allergen. However, some individuals may exhibit evidence of immune sensitisation to non-food environmental allergens, while others may suffer from both PFI and FA, though not to the same food. In either of these scenarios, an individual may misattribute their symptoms to an allergic reaction and eliminate the food. Findings from a recent

systematic review (see Chapter 1) suggests an association between PFI and immune-mediated conditions, including manifestations of atopy such as asthma, allergic rhinitis and eczema (ibid), and the autoimmune condition rheumatoid arthritis (Liden, Kristjansson, Valtysdottir, Venge, & Hllgren, 2010). Further, some individuals with PFI may exhibit immune activation alongside food, as the immune system can be modulated by the stress response, which can contribute to GI symptoms through intestinal mast cell activity (Mayer, 2000; Mayer, Naliboff, Chang, & Coutinho, 2001). This perhaps could contribute to a conditioned response to food and the misidentification of PFI, though requires further investigation.

It is important to note that the immune system can produce non-IgE antibodies in response to food, such as IgG antibodies and their subclass IgG₄. IgG has been reported to rise in both allergic and healthy non-allergic individuals following ingestion of a food, and should not be interpreted as indicative of PFI nor FA (Gocki & Bartuzi, 2016; Stapel et al., 2008). Despite this, there are a large number of direct-to-consumer IgG antibody blood tests, though evidence consistently concludes that these are not recommended to be used as they have a high false positive rate (Sicherer & Sampson, 2018; Stapel et al., 2008; Teuber & Porch-Curren, 2003). A position statement from the Canadian Society of Allergy and Clinical Immunology (CSACI) on the testing of IgG highlights how these tests may lead to false positives which can result in unnecessary dietary restrictions and reduced QoL (Carr, Chan, Lavine, & Moote, 2012). Further, the financial burden and risk of a false positive not only falls on the consumer, who may needlessly eliminate nutritious and innocuous foods, but may have subsequent consequential effects on healthcare system costs as individuals with positive results may request specialist referrals and further costly investigations (Carr et al., 2012).

1.2.2 Enzymatic, Pharmacological, and Additional Mechanisms

In PFI, pathology is often difficult to establish and may be mediated through enzymatic, pharmacological and additional undefined mechanisms (Ortolani & Pastorello, 2006; Skypala, 2011; Zopf et al., 2009). These mechanisms are not easily evidenced and

compounded by the inherent challenge that PFI reactions are delayed and may not appear for hours or days after exposure to the offending food.

PFI reactions may be mediated by mechanisms such as enzymatic deficiencies such as the β -galactosidase deficiency implicated in lactose intolerance, pharmacological mechanisms such as those implicated in salicylate, caffeine and biogenic amine (e.g. histamine) intolerance, and additional undefined mechanisms that are still not well understood, such as unknown mechanisms in food additive intolerance (Ortolani & Pastorello, 2006; Skypala, 2011; Tuck, Biesiekierski, Schmid-Grendelmeier, & Pohl, 2019).

A study by Litleskare et al. (2015) concluded that exposure to *Giardia* was associated with reported PFI. GI infection has been evidenced as a risk factor in Irritable Bowel Syndrome (IBS) (Gwee, 2010; Litleskare et al., 2015; Thabane & Marshall, 2009). Additionally, PFI was reported by those with *Helicobacter pylori* positive dyspepsia (Olafsson & Berstad, 2003), but to the authors knowledge, associations between infection and PFI has not been described elsewhere. Finally, it is possible that changes in intestinal physiology, including mucosal inflammation, intestinal permeability, microbiota, or intestinal mast cells may be implicated in PFI, though this is outside the scope of the current study (Lillestøl, Helgeland, et al., 2010; Nybacka et al., 2018).

1.2.3 Comorbid Clinical Factors

Individuals with PFI experience GI symptoms including GI distress (bowel changes of constipation and diarrhoea), bloating and discomfort, and extraintestinal symptoms including fatigue, headaches, musculoskeletal pain, and skin reactions. Nonspecific symptoms have also been described, including dizziness, irregular menstrual periods (Manu, Matthews, & Lane, 1993), confusion, memory difficulties, and difficulty sleeping (Parker, Leznoff, Sussman, Tarlo, & Krondl, 1990). There is considerable symptom overlap between PFI and functional gastrointestinal disorders (FGID) including dyspepsia and IBS. A large proportion of patients with IBS report PFI, and similarly, in clinical samples of those suspected to have PFI, 71% - 99% met criteria for IBS (see Chapter 1). Further, PFI has been described in clinical samples with chronic fatigue (Manu et al., 1993), and individuals with PFI have self-reported chronic fatigue and fibromyalgia (Berstad, Undseth, Lind, &

Valeur, 2012; Jakobsen, Braaten, Obstfelder, & Abelsen, 2016; Lind, Berstad, Hatlebakk, & Valeur, 2013).

Key findings from a qualitative study established ‘persistent physical symptoms’ (Picariello, Ali, Moss-Morris, & Chalder, 2015) as the preferred term to refer to symptoms and conditions without current medical explanation, and individuals can often experience symptom overlap between these conditions (Aaron & Buchwald, 2001; McKenzie, Oto, Graham, & Duncan, 2011; Nimnuan, Hotopf, & Wessely, 2001). Persistent physical symptoms (Picariello et al., 2015) cause functional impairment yet despite medical examination, have no organic pathology and typically respond poorly to medical intervention (Chalder & Willis, 2017; Rosendal et al., 2017). They are associated with elevated distress and are frequently seen within medical specialties and primary care, contributing to increased healthcare visits and costs (Barsky, Orav, & Bates, 2005; Rosendal et al., 2017). It is possible that reported comorbidities and symptom overlap between PFI, IBS and other persistent physical symptoms represents shared mechanisms, and there are similarities between PFI and IBS that warrant further investigation.

1.3 Psychological and Cognitive Factors Associated with PFI

1.3.1 Affect, Personality and Worries

Previous research investigating psychological characteristics of individuals with PFI has focused on characteristics including negative affect (anxiety, depression, and general psychological distress), personality traits, and characteristics of worries, though most studies conducted to date have been at a cross-sectional bivariate level, which precludes understanding of the relationship between these factors and PFI, and what other variables may be contributing to any relationship described (see Chapter 1). Evidence is largely mixed, and some studies have determined that there are increased self-reports of anxiety, depression, and distress versus non-patients (see Chapter 1), though this rarely reached clinical threshold and was often investigated in clinical samples, which limits generalisability. Research examining personality traits including neuroticism is inconsistent (Golley et al., 2015; Knibb, Armstrong, et al., 1999; Lillestøl, Berstad, et al.,

2010), and findings are limited by methodological quality, including using one-time surveys (Golley et al., 2015; Knibb, Armstrong, et al., 1999; Lillestøl, Berstad, et al., 2010), infrequently used measures (Golley et al., 2015), and self-selected clinical samples (Lillestøl, Berstad, et al., 2010). Evidence suggesting a role of symptom anxiety (Böhn, Störsrud, Törnblom, Bengtsson, & Simrén, 2013; Lind, Lied, Lillestøl, Valeur, & Berstad, 2010) and health anxiety (Elieson et al., 2017; Golley et al., 2015) in PFI has not been thoroughly explored, and results were conflicting and all of poor quality (see Chapter 1). Finally, there has been a paucity of research examining specific beliefs that may contribute to PFI. Limited research in individuals with PFI has determined that general worries relating to modern health are not significant (Elieson et al., 2017; Lind et al., 2005), though food-related worries about genetically modified foods were characteristic in PFI (Lind et al., 2005), however, the measure used in these studies did not capture how these beliefs relate to PFI specifically, or if they influence outcome. The results demonstrate that at this point, we are currently not able to draw solid conclusions about the role of affect, personality or cognitions as contributing to PFI.

1.3.2 Somatic Symptoms

Evidence consistently indicates that individuals with PFI report significantly more somatic symptoms and increased symptom severity than individuals without PFI (see Chapter 1). It is likely that symptoms in PFI are not mediated through pathways implicated in FA, and symptom overlap with FGID including IBS and persistent physical symptoms alludes to potential shared mechanisms (Berstad, Arslan, Lind, & Florvaag, 2005; Berstad et al., 2012; Böhn et al., 2013; Dainese et al., 2014; Dainese, Galliani, Lazzari, Leo, & Naccarato, 1999; Frissora & Koch, 2005; Lied et al., 2011; Lillestøl, Berstad, et al., 2010; Lind et al., 2005; Lind, Lied, et al., 2010; Lind, Lillestøl, et al., 2010; Monsbakken, Vandvik, & Farup, 2006).

Persistent physical symptoms were historically thought of as a psychosomatic syndrome whereby physical symptoms are manifestations of stress or psychological distress (Lipowski, 1986). However, theories exploring the role of the cognitive and behavioural interactions have since been proposed to contribute to the experience and

maintenance of persistent physical symptoms, including sensitisation, illness representations and related coping strategies (Brosschot, 2002; Eriksen & Ursin, 2002; Eriksen & Ursin, 2004; Knowles et al., 2017; Moss-Morris & Chalder, 2003; Moss-Morris, Petrie, & Weinman, 1996; Ursin & Eriksen, 2001; Yunus, 2007, 2008).

1.3.3 Sensitisation and Related Theories

Sensitisation refers to an elevated response due to increased use or stimulation (Eriksen & Ursin, 2002; Eriksen & Ursin, 2004; Petrie et al., 2001). Sensitisation has been proposed to contribute to physiological sensations and pain through mechanisms of central sensitivity and visceral sensitivity in the central and peripheral nervous systems (Bueno, Fioramonti, Delvaux, & Frexinos, 1997; Mayer & Raybould, 1990; Yunus, 2007, 2008). The theory of sensitisation has been likened to higher-order processes of attentional and cognitive biases, whereby perceiving or experiencing increased threat will lead to the detection of more threat, and has been expanded to account for the experience and reporting of somatic symptoms in persistent physical symptoms (Brosschot, 2002; Eriksen & Ursin, 2002; Eriksen & Ursin, 2004; Ursin & Eriksen, 2001).

Brosschot (2002)'s theory of cognitive-emotional sensitisation hypothesises that individuals who are concerned about symptoms or an illness can develop a cognitive bias towards all illness relevant information. This bias is strengthened by illness-specific worries leading to an increased focus and awareness of symptoms, activation of cognitive networks that result in misattributions and over-reporting of bodily symptoms, influencing the development of a 'cognitive-emotional sensitisation' (Brosschot, 2002). Sensitisation assumes a degree of specificity of the triggering mechanism, as specific illness-related worries and fears activate these cognitive networks. A construct of GI symptom-specific anxiety (GSA) has been proposed to contribute to symptomatology in IBS. GSA is formed from conceptualisations of anxiety sensitivity, and posits the role of specific worry, fear, hypervigilance, visceral sensitivity and responses to GI sensations as contributing to the maintenance of IBS (Labus et al., 2004; Labus, Mayer, Chang, Bolus, & Naliboff, 2007; Porcelli, De Carne, & Leandro, 2014), and preliminary evidence additionally shows a role of GSA in PFI (Lind, Lied, et al., 2010). These types of cognitive

bias have been considered previously, forming the model of somatosensory amplification; a construct that reflects cognitive and attentional biases to selectively attend to somatic sensations and experience them as pathological, which can enhance their perception, generation, and can influence how symptoms are experienced (Barsky, 1979; Barsky, Goodson, Lane, & Cleary, 1988; Barsky, Wyshak, & Klerman, 1990). Research has implied that somatosensory amplification influences frequency of reported symptoms in FGID (Jones & Ebert, 2003; Jones, Schettler, Olden, & Crowell, 2004), and there is limited evidence in PFI, though methodologically of poor quality (Elieson et al., 2017).

The cognitive-emotional sensitisation theory (Brosschot, 2002) was extended to PFI by Berstad et al. (2005), who suggested individuals with PFI will develop a cognitive and attentional bias. This increases vigilance towards, and detection of PFI-related or ambiguous information (including thoughts, symptoms and food), and consequently influences the misattribution and misappraisal of the information, over-reporting of somatic symptoms and a tendency to over-interpret ambiguous information as in-line with their beliefs. This results in a cycle where repeated activation of these networks through 'scanning' for PFI-related information can lead to continued 'threat detection', and the start of another cycle, and may also influence resultant behaviour, including reporting symptoms and avoiding foods, which could be targeted in a behavioural intervention (Berstad et al., 2005)

The role of sensitisation is hypothesised to contribute to persistent physical symptoms including IBS and chronic pain conditions, and recently the theory of cognitive-emotional sensitisation has been proposed in PFI. There is some cross-sectional data implying a role of somatosensory amplification (Elieson et al., 2017) and GSA (Lind, Lied, et al., 2010) in PFI, however, these studies are not easily generalised, are limited by small, self-selected samples, and Elieson et al.'s (2017) study has several methodological issues (see Chapter 1). Specific PFI-beliefs and appraisals that activate cognitive networks and contribute to the development of a cognitive bias are not yet known, or how they relate to coping and outcome. This information is crucial in order to identify processes that might maintain PFI, which can be targeted in a multifaceted psychological intervention.

1.3.4 Illness Perceptions and the Common-Sense Model of Self-Regulation

The beliefs an individual holds about their condition contributes to the development of a cognitive representation of the condition, which has a significant impact on behaviours relating to coping and self-management (Moss-Morris et al., 2002; Petrie, Jago, & Devcich, 2007; Petrie & Weinman, 2006). This schema is formed of specific thoughts or ‘illness perceptions’, as posited by the common-sense model of self-regulation (CS-SRM/CSM) (Leventhal, 1984) and measured by the Illness Perception Questionnaire (IPQ) (Weinman, Petrie, Moss-Morris, & Horne, 1996).

The CSM provides a framework for understanding the processes involved in managing health and illness threats (Leventhal, Phillips, & Burns, 2016). The model suggests individuals facing an illness threat will construct specific and parallel cognitive and emotional representations in order to provide a framework that underlies the appraisal of illness-related information, derives meaning about that information, and guides subsequent “action plans” that influence outcomes such as coping responses, mood, possible treatments and self-management behaviours (Leventhal, Brissette, & Leventhal, 2003; Leventhal et al., 2016). The CSM benefits from a dynamic framework whereby illness perceptions can integrate with new health-threat knowledge and feedback obtained from the appraisal of management behaviours. This information can support or update representations to guide and appraise subsequent actions, thus providing a process for the ‘self-regulation’ of illness perceptions and health behaviours (Leventhal et al., 2016).

In the original CSM, illness representations were divided into five core domains; *identity* (the label placed on the condition and perceptions of associated symptoms), *consequences* (perceived physical, social, economic and emotional consequences of the condition), *cause* (beliefs about factors responsible for the condition whether internal, external or environmental), *control/cure* (beliefs about the extent to which the condition can be cured or controlled), and *timeline* (beliefs about the length of time the condition will last, which can be considered to be acute or chronic) (Leventhal, 1984; Leventhal et al., 2003; Leventhal et al., 2016). However, three additional constructs were included in

the 2002 revision of the IPQ (IPQ-R) (Moss-Morris et al., 2002); *emotional representations* (emotional impact of and in response to the condition), *coherence* (extent to which the individual has a coherent understanding of their condition), and *cyclical timeline beliefs* (beliefs about changeability and unpredictability of the condition). Further, the control domain was separated into two subscales: *personal control* and *treatment control*. The IPQ-R provides a greater understanding of the role of an individual's illness perceptions, allowing for the parallel and multi-level measurement of cognitive and emotional reactions to illness-related information and providing information on the underlying processes influencing outcome.

The CSM has been applied to various physical health conditions reported alongside PFI, including chronic pain, chronic fatigue, rheumatoid arthritis and asthma (Foster et al., 2008; Kaptein, Klok, Moss-Morris, & Brand, 2010; Moss-Morris & Chalder, 2003; Moss-Morris et al., 1996; Scharloo et al., 1998), and in IBS and allergy, conditions which have symptom and outcome overlap with PFI (Chilcot & Moss-Morris, 2013; De Gucht, 2015; Knowles et al., 2017; Rutter & Rutter, 2002, 2007). However, to the authors knowledge, illness perceptions have not yet been investigated in PFI.

Illness perceptions can influence self-management behaviours and research has demonstrated that coping may mediate reported outcome, including distress, somatic symptoms, functioning, and QoL (De Gucht, 2015; Knibb & Horton, 2008; Knowles et al., 2017; Moss-Morris et al., 1996). In allergy populations, the CSM was used to explain adherence to treatment behaviours in adolescents with FA (Jones et al., 2014), concluding those with stronger *illness identity* and *emotional representations* of FA were more likely to adhere to self-care behaviours, whereas increased *timeline cyclical beliefs* were associated with poorer adherence. Additionally, illness perceptions were reported to explain between 6 – 26% of the variance on measures of distress in adults with any form of allergy (Knibb & Horton, 2008). Knibb and Horton (2008) further concluded strong *illness identity*, *consequences* and *emotional representations* were associated with increased distress and somatic symptoms, and strong *personal control* beliefs were associated with fewer somatic symptoms and decreased distress. However, as this was a

cross-sectional study and not prospective; i.e. participants were not recruited at their symptom onset, it is not possible to know the direction of the findings, as increased distress and symptom severity could equally influence illness representations.

The CSM has been substantiated in conditions which are both relevant and related to PFI, to help explain factors that contribute to adjustment, self-management and outcome. To the authors knowledge, cognitive and emotional representations of PFI have not yet been investigated, and so it is difficult to draw conclusions about how individuals with PFI think about and manage their condition, or if they even perceive it to be a condition. The current study will explore the CSM in relation to PFI, to better understand how individuals perceive and respond to PFI and how this influences outcome.

1.3.5 Coping

Coping includes both cognitive and behavioural responses and strategies when faced with a perceived threat to help manage (reduce, tolerate, or master) the threat (Lazarus, 1990; Lazarus & Folkman, 1984). According to the theory of stress and coping (Folkman, Lazarus, Dunkel-Schetter, DeLongis, & Gruen, 1986; Lazarus, 1990; Lazarus & Folkman, 1984), coping ultimately determines adaptational and functional outcome, and was originally considered as coping styles, to be either *emotion-focused* (used to regulate distressing emotions) or *problem-focused* (used to initiate problem-solving or 'change') (Folkman & Lazarus, 1985). This view was eventually expanded to account for various coping strategies that an individual uses and instruments such as the Coping Orientation to Problems Experienced (COPE) scale were developed by Carver, Scheier, and Weintraub (1989). The COPE incorporated 14 domains of coping clustered into two groups; those that are theoretically more adaptive and those that may not be as functional (Carver et al., 1989). Subsequent research using the COPE has suggested strategies such as *denial*, *behavioural disengagement* and *mental disengagement* were associated with increased distress whereas strategies including *positive reframing*, *acceptance*, *planning* and *seeking emotional support* were associated with decreased distress and better adjustment (Carver, 1997; Carver et al., 1993; Carver & Scheier, 2002; Knibb & Horton, 2008; Moss-Morris et al., 1996). A cross-sectional community study with adults with all

forms of allergy found that lesser use of coping including *positive reinterpretation, acceptance, active coping* and *planning* and increased use of strategies such as *focusing on and venting emotions* were associated with elevated stress and anxiety (Knibb & Horton, 2008), however, the design of this study precludes drawing conclusions about the nature or direction of these relationships.

While the use of coping scales such as the COPE (Carver et al., 1989), its abbreviated version (the Brief-COPE) (Carver, 1997), and other measures have been widely used in research, coping scales have been criticised for not all representing similar coping constructs and strategies, which makes comparing results from studies using differing scales difficult (Skinner, Edge, Altman, & Sherwood, 2003). Furthermore, scales that measure specific coping strategies often do not account for the adaptive nature and dynamic context in which the strategies are used, and there are various antecedents and contextual considerations that are not accounted for (Skinner et al., 2003; Taylor & Stanton, 2007).

It is important to explore the range of coping strategies that appear to be significant in PFI, however, it is necessary to hold that this would not provide a full understanding of coping in PFI. A better understanding of the role of coping strategies might help explain the relationship between illness perceptions and outcome, as coping potentially has a mediating role, as posed by the CSM (Leventhal, 1984). Further, an initial understanding of coping in PFI can contribute to an informed psychological intervention by elucidating additional components necessary to include in intervention.

1.3.6 Health-Related Behaviours

Research suggests that individuals with PFI experience distress and somatic symptoms in relation to their intolerance, and it is possible that this might contribute to reported changes in health-related behaviours. Those with PFI are more likely to self-diagnose, alter their eating habits, avoid specific foods or food groups, or completely eliminate perceived triggering foods (Biesiekierski et al., 2014; Blackett, Shamsunder, Reilly, Green, & Lebowhl, 2018; Fitzgerald & Frankum, 2017; Knibb et al., 2000; McGowan & Gibney, 1993; Sommer, MacKenzie, Venter, & Dean, 2012). In a community-based

study, Knibb et al. (2000) found that individuals with PFI were more likely to take time off work and change their eating habits by avoiding or reducing the offending food than controls, and were less likely to have been professionally advised about altering their diet. Further, in a sample of individuals reporting PFI, McGowan and Gibney (1993) reported that 34% diagnosed themselves, and 57% reported that they nearly always avoid the food(s) in question. Undertaking restrictive and/or avoidant diets may impact general health including nutrient deficiencies and their sequelae (McGowan & Gibney, 1993). Further, the experience of PFI and the potential for consequential food avoidance may negatively impact on relationships with food (Böhn et al., 2013), lead to excessive concern and worry relating to food, and could potentially influence the development of disordered eating behaviours. Preliminary research has found mixed evidence for associations between PFI and orthorexia nervosa (McComb & Mills, 2019; Missbach et al., 2015), and an association between PFI and avoidant/restrictive food intake disorder (Fitzgerald & Frankum, 2017). The tendency for individuals with PFI to self-diagnose and engage in restrictive/avoidant behaviours as a result of their PFI provides insight into how these individuals self-manage their condition. There is evidence that PFI is associated with poorer QoL (Arslan et al., 2004), however, we do not know how individuals with PFI perceive their food-related QoL (FR-QoL). Food and meals, and psychosocial aspects surrounding food and meals are an important component of daily living and may be associated with distress for those with PFI, who may have to be more careful about what they eat and where they can eat (for example, meals out, eating meals 'on-the-go', when travelling, or at friends or relatives houses), and may be more worried about the impact of food and meals on symptoms.

Research exploring FR-QoL in PFI, to the authors knowledge, does not exist, though FA QoL scales for children and parents have been developed and validated (Factor, Mendelson, Lee, Nouman, & Lester, 2012). Following oral desensitisation in children with peanut allergy, Factor et al. (2012) described improved FR-QoL including in emotional impact, food-related anxiety, social and dietary limitations, dietary restriction, and risk of accidental exposure. In IBS, Böhn et al. (2013) established that those who reported more

food-related symptoms had poor QoL. Guadagnoli et al. (2019) found that individuals who undertook dietary treatments (including food elimination and avoidance) had decreased FR-QoL, and additionally reported that individuals with IBS had poorer FR-QoL than individuals with Inflammatory Bowel Disease (IBD), which refers to chronic and inflammatory GI conditions including Crohn's disease and ulcerative colitis. In IBD, FR-QoL is considered a significant patient-related outcome, and a specific FR-QoL measure has been developed and validated (Hughes et al., 2016). Recent qualitative evidence from individuals with IBD indicates that various psychosocial aspects of life impact FR-QoL, and patients often use trial-and-error to alter their diets in the hopes of improving the impact, though often without success (Czuber-Dochan et al., 2020). It is important to consider that PFI and IBD are very different conditions, though food plays a significant role in patient-related outcome in IBD (Hughes et al., 2016), and as food is believed to be a significant cause of symptoms in PFI, it is possible that FR-QoL is important in PFI.

Further, it is plausible that illness perceptions and coping impact FR-QoL as an outcome. The beliefs an individual with PFI holds about their intolerance and resulting coping strategies used in the context of food or meal-related situations may affect FR-QoL, though this is not known. Food avoidance and restriction can be targeted through a behavioural component of a psychological intervention (Berstad et al., 2005), but better understanding the impact and contributors of PFI in FR-QoL will determine if this is a necessary component of an intervention.

1.4 Summary

PFI is a distressing yet largely unexplained condition that affects a significant proportion of the population (when compared with FA) and is often reported by women. Although there is a substantial body of literature examining the pathophysiological, psychological, and health related factors associated with FA, factors associated with the maintenance of PFI are understudied and remain largely unknown, despite the documented substantial personal and societal costs of PFI.

It is likely that PFI is the result of multiple interactions between biological mechanisms, psychological, cognitive and psychosocial factors. Alongside enzymatic, pharmacologic and additional undefined mechanisms, it is possible that infection, changes in intestinal physiology, and the stress response may contribute to factors associated with the onset of PFI. Research investigating psychological characteristics in PFI concludes individuals with PFI report frequent and severe somatic symptoms, and it is possible that sensitisation mechanisms proposed to underlie related persistent physical symptoms may additionally be implicated in PFI. Previous research additionally reports increased distress as compared to those without PFI. Distress may be influenced by factors such as illness perceptions, coping, self-management behaviours and consequences of PFI, though this requires further investigation

1.5 Rationale and Aims

There is a need to further examine psychological and additional PFI-related factors in adults with PFI, to better understand how these factors may interact to influence cognitive appraisals, coping, affect and outcome. Given the strength of the CSM in identifying an individual's beliefs about their illness, and its recent substantiation in allergy populations, we are interested in whether the CSM is an appropriate model to apply in a PFI population. It is important to identify modifiable factors that may contribute to the maintenance of PFI over time, in order to develop a targeted and multifaceted psychological intervention to improve outcome. Future intervention could be based on Cognitive Behaviour Therapy (CBT), which aims to help an individual identify unhelpful beliefs and behaviours and challenge assumptions, or Acceptance and Commitment Therapy (ACT), a contextual form of CBT which aims to increase psychological flexibility and engage in values-directed actions. Both have the anticipated outcome of managing distress, increasing use of flexible coping strategies and improving functioning.

Research to date is mixed, with several methodological issues. Data are predominantly cross-sectional and conducted at the bivariate level, which does not provide information as to how symptoms, distress and impact change over time, and

precludes casual inferences about the factors associated with PFI. The present study was a longitudinal exploratory study that aimed to explore whether applying the CSM provides a theoretical framework that can help advance this research, and further, to identify significant and modifiable factors that could be targeted in an intervention. We investigated whether PFI-related illness perceptions and coping strategies influenced negative affect and FR-QoL and explored additional factors that contribute to PFI. The results of this study will help to improve understanding of the lived experience of food intolerance, which additionally may provide health care professionals with information that can be helpful for their patients, and in their own understanding of their patient's complaints. Additionally, we aimed to identify modifiable factors that may maintain distress in PFI, in order to work towards the development of a model and related psychological intervention to improve outcome

1.6 Hypotheses

The study is exploratory, and thus all hypotheses (PH) and aims (PA) are exploratory.

Primary Hypotheses:

- PH1) To explore and identify any illness perceptions associated with negative affect (anxiety and distress) and poor FR-QoL, using bivariate and multivariate analyses.
 - Based on previous research in IBS (Rutter & Rutter, 2002) and allergy (Knibb & Horton, 2008), we expect illness representations including illness identity, emotional representations, and consequences beliefs to be associated with negative affect (anxiety and distress) and poorer FR-QoL, and improved illness coherence and control beliefs to be associated with improved affect (anxiety and distress) and FR-QoL.
- PH2) To explore and identify coping strategies associated with negative affect (anxiety and distress) and poor FR-QoL, using bivariate and multivariate analyses.
 - Based on previous research in IBS (Rutter & Rutter, 2002) and allergy (Knibb & Horton, 2008), we expect that coping strategies such as acceptance, positive

reinterpretation and planning will be associated with improved affect (anxiety and distress) and FR-QoL, and that strategies including self-blame and disengagement will be associated with decreased affect (anxiety and distress) and poorer FR-QoL.

- PH3) To explore and identify additional psychological and PFI-related factors associated with negative affect (anxiety and distress) and poor FR-QoL, including perceived stress, symptom severity, functional impairment, and severity of PFI (measured by the number of offending foods reported), using bivariate and multivariate analyses.

Primary Exploratory Aims:

To assess the stability of illness perceptions, coping strategies and impact of PFI over time, in order to:

- PA1) To explore the mediating relationship of illness perceptions (T1) and coping (T1), on negative affect and poor FR-QoL at T2, to determine whether the CSM is an appropriate model to apply to PFI.
- PA2) To explore the mediating relationship of additional psychological and PFI-related factors (T1), illness perceptions (T1) and coping responses (T1), on negative affect and poor FR-QoL at T2.

Secondary Exploratory Aim:

- SA1) To explore the lived experience of PFI, using content analysis from information provided by participants in the free-text box of the questionnaire.

2 Methods

2.1 Design

An observational longitudinal design was employed, and data were collected at three timepoints; baseline (T1), 3-months post-baseline (T2), and 6-months post-baseline (T3). A within-groups design was used to assess illness perceptions, coping strategies, negative affect, FR-QoL, perceived stress, functional impairment, and symptom severity, to understand if these remain relatively stable, or fluctuate over time.

To assess primary hypotheses and aims, the primary dependent variables included anxiety as measured by the HADS-A, total distress (HADS-T) (Zigmond & Snaith, 1983), and FR-QoL as measured by the Satisfaction with Food Related Life Scale (SWFL) (Grunert, Dean, Raats, Nielsen, & Lumbers, 2007). The primary independent variables were (PH1) CSM constructs as measured by the IPQ-R (Moss-Morris et al., 2002), (PH2) coping responses as measured by the Brief-COPE (Carver, 1997), and (PH3) additional psychological and PFI-related factors including scores from outcome measures (*see 2.5.2*) and severity of PFI (number of foods intolerant to).

The study was conducted entirely online, involving administering a purpose-designed questionnaire on the platform Qualtrics (<https://www.qualtrics.com/uk/>), which was completed at three timepoints; baseline (T1), 3-month follow-up (T2), and 6-month follow-up (T3). Covariates will include age and gender if significant.

2.2 Power Analysis

A power analysis was conducted in GPower (Faul, Erdfelder, Lang, & Buchner, 2007). Power was set at 0.8, $\alpha = 0.05$, and indicated a sample size of 150 patients was required to detect a moderate effect size of .30, if we were to use all variables entered into a regression model (distress, Brief-COPE domains, and IPQ-R constructs). To account for 40% attrition over time, the aim was to recruit a sample of $N = 210$, to ensure the study would be sufficiently powered to detect significant predictors, assuming all Brief-COPE domains and IPQ-R constructs were significant. However, our intent was to only use

only Brief-COPE domains and IPQ-R factors demonstrating significance from correlational analysis.

2.3 Ethical Approval

Ethical approval for this study (HR-18/19-8576) was granted by the King's College London Psychiatry, Nursing and Midwifery Research Ethics Subcommittee on 27th February, 2019 (see Appendix I). As this project required participants to consider whether they have experienced low mood or anxiety, information regarding sources of support was provided in the study information sheet (see Appendix II), which participants were asked to read before they were able to proceed to accessing the study consent form (see Appendix III). An amendment to add the Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1994) was approved on 07/05/2019, prior to data collection.

2.4 Participants and Setting

Participants were adults living in the United Kingdom and were recruited online via targeted advertisements via social media, and an advert in the King's College London (KCL) Research Ethics Committee fortnightly circular recruitment email. Three hundred and forty-nine adults provided consent to participate study, and of these, three hundred and thirty-three completed the questionnaire at baseline.

2.4.1 Inclusion and Exclusion Criteria

Potential participants were eligible if they were over the age of 18; fluent in English; had access to the internet to complete a survey; and self-reported PFI (participants were not subjected to an oral food challenge to confirm their PFI). Potential participants were excluded if they had a medically-diagnosed FA only; were acting as a proxy for a child's symptoms; were under the age of 18; and were not fluent in English. Exclusion criteria were determined based on the study aim to investigate the individual's subjective experience of PFI in the general population, and as a parent or carer's interpretation of an individual's experience are not equivalent to the individuals subjective experience. Further, the questionnaire was written in English and administered

over a web-based survey, and for convenience and comprehension purposes the decision was made to only include adults fluent in English.

2.5 Study Questionnaire

2.5.1 *Demographic and Clinical Information*

A purpose-designed questionnaire was built (see Appendix IV) including i) basic demographic information; age, identified gender, ethnicity (ONS categories), ii) PFI-related information; a list of 10 clinically recognised common PFI foods, a list of symptoms typically reported in PFI, how PFI was diagnosed, age at which symptoms appeared, iii) FA-related information; list of 10 clinically recognised allergenic foods, list of symptoms typically reported in FA, how FA was diagnosed, use of epi pen, age symptoms appeared, iv) additional health information; diagnosis of IBS, Coeliac Disease, and any atopic condition. A free text box was included for participants to discuss how PFI affects their life. Items were drafted using careful consideration for question type, wording and layout, matching response options to questions and applicability of the survey questions to the study objective and the participants and was assessed by a focus group of service-users to obtain feedback prior to study recruitment (see 2.7).

2.5.2 *Outcome Measures*

The Revised Illness Perception Questionnaire (IPQ-R) (Moss-Morris et al., 2002). The IPQ-R is a validated measure of an individual's illness perceptions across 8 subscale factors, including identity, consequences, personal control, treatment control, timeline acute/chronic beliefs, timeline cyclical beliefs, illness coherence and emotional representations. Illness identity is measured by the sum-score of items where an individual indicates whether they believe symptoms are related to their illness. The remaining subscale factors are measured through a 38 items questionnaire, rated on a five-point Likert scale from 1 (strongly disagree) to 5 (strongly agree). The IPQ-R additionally measures beliefs about the cause of the condition. Items are considered individually and do not have a sum score. The IPQ-R was adapted for the current study;

the word 'illness' was replaced with 'intolerance', and a symptom of 'brain fog' was added, as it has been reported in PFI. In the current sample, reliability analysis on the 38-item scale demonstrated acceptable internal consistency ($\alpha = .77$), and analyses on subscale factors of *consequences* ($\alpha = .86$), *personal control* ($\alpha = .80$), *treatment control* ($\alpha = .80$), *timeline acute/chronic* ($\alpha = .88$), *timeline cyclical* ($\alpha = .88$), *illness coherence* ($\alpha = .92$) and *emotional representations* ($\alpha = .91$) demonstrated good internal consistency.

The Brief COPE Inventory (Brief-COPE) (Carver, 1997). The Brief COPE is a validated 28-item questionnaire to measure a range of coping responses and is an abbreviated version of the original 60-item COPE Inventory. The Brief-COPE consists of 14 subscales, which each reflect different coping responses, including *self-distraction*, *active coping*, *denial*, *substance use*, *use of emotional support*, *use of instrumental support*, *behavioural disengagement*, *venting*, *positive reframing*, *planning*, *humour*, *acceptance*, *religion*, and *self-blame*. All 28 items are scored on a four-point Likert scale from 1 ('I haven't been doing this at all') to 4 ('I've been doing this a lot'), and 2 items are combined to compute each of the 14 subscale factors. In the current sample, reliability analyses on all scale items demonstrated good internal consistency ($\alpha = .88$), however, internal consistency of the subscales varied, ranging from ($\alpha = .44$) '*substance-use*' to ($\alpha = .89$) '*use of instrumental support*'.

The Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). The HADS is a 14-item reliable and validated scale to assess anxiety (HADS-A) and depressive (HADS-D) symptoms, with 7 items allocated to each subscale. Item responses are unique to the question and scored on a four-point scale from 0 to 4, with higher scores being indicative of increased severity of anxiety or depression symptoms. Clinical cut-off scores for both subscales are set at a score of ≥ 8 . The total score (HADS-T) is the sum of all 14 items. In populations with persistent physical symptoms, the HADS-T has been demonstrated to be a particularly useful way to measure general psychological distress (Norton, Cosco, Doyle, Done, & Sacker, 2013). Further, the HADS is often used in clinical populations as few items reference somatic symptoms in order to provide a reliable measure of mood as opposed to a measure of the impact of somatic symptoms such as

fatigue, pain or insomnia (Bjelland, Dahl, Haug, & Neckelmann, 2002; Johnston, Pollard, & Hennessey, 2000; Norton et al., 2013; Zigmond & Snaith, 1983). In the current sample, reliability on the anxiety and depression subscales demonstrated good internal consistency ($\alpha = .872$) and ($\alpha = .856$) respectively, and reliability of all scale items (HADS-T) demonstrated strong internal consistency ($\alpha = .90$).

The Satisfaction with Food-Related Life (SWFL) (Grunert et al., 2007). The SWFL scale is a short, unidimensional, and valid 5-item measure of food related QoL. All items are scored on a seven-point Likert scale from 1 (strongly disagree) to 7 (strongly agree), for a maximum sum score of 35 (indicative of being extremely satisfied with food-related life). In the current sample, reliability analysis on all scale items demonstrated good internal consistency ($\alpha = .88$).

The Perceived Stress Scale (PSS) (Cohen et al., 1994). The perceived stress scale is a reliable and validated 10-item measure of the degree to which an individual perceives events as stressful. Items are rated on a 5-point scale from 0 (never) to 4 (very often), for a maximum sum score of 40. Higher scores are indicative of increased perceived stress. A review concluded the psychometric properties of the 10-item PSS is superior to those of the 14-item and 4-item PSS, with good internal consistency reported (Lee, 2012). In the current sample, reliability analyses demonstrated poor internal consistency ($\alpha = .20$).

The Work and Social Adjustment Scale (WSAS) (Mundt, Marks, Shear, & Greist, 2002). The WSAS is a reliable and validated 5-item scale measuring functional impairment, to assess the impact of an individual's difficulties across five domains; work, home management, social leisure activities, private leisure activities, and relationships. Items are rated on a nine-point Likert scale from 0 (not at all impaired) to 8 (very severely impaired), for a maximum sum score of 40. Clinical cut-off on the WSAS is established ≥ 10 , corresponding to significant functional impairment. In the current sample, reliability analysis demonstrated strong internal consistency ($\alpha = .94$).

The Patient Health Questionnaire (PHQ-15) (Kroenke, Spitzer, & Williams, 2002). The PHQ-15 is a self-administered reliable and valid questionnaire used to assess the severity of fifteen somatic symptoms. Each symptom is scored from 0 (not bothered at

all) to 2 (bothered a lot). Cut-off scores of 5, 10 and 15 have been set to represent low, medium and high symptom severity. In the current sample, reliability analysis demonstrated good internal consistency ($\alpha = .86$).

The Birmingham IBS Symptom Questionnaire (IBS-SQ) (Roalfe, Roberts, & Wilson, 2008). The Birmingham IBS Symptom Questionnaire is an 11-item validated scale based on Rome-II criteria to assess the severity of IBS symptoms. Items are scored on a 6-point Likert scale ranging from 0 ('none of the time') to 5 ('all of the time'), which derives a sum scale score, and score for three subscales measuring specific symptoms of 'diarrhea', 'pain', and 'constipation'. Scores are calculated specifically for each subscale the total sum score, which provide a score out of 100. Previous research has demonstrated acceptable reliability and good test-retest reliability, and reliability in the currently sample demonstrated good internal consistency ($\alpha = .85$).

2.6 Procedure

The Qualtrics platform was used to collect data from the purpose-built questionnaire. The questionnaire was comprised of four sections; 1) participant information sheet, 2) eligibility criteria, 3) consent form and 4) the study questionnaire, which included a section on demographic and clinical information (see 2.5.1), followed by all outcome measures. At the end of the questionnaire, a free text box was included for participants to write anything about their PFI that they wished to share. The main study questionnaire was only accessible to those who completed the consent form and met all eligibility criteria. The questionnaire was developed and shared with a recruited focus-group, comprised of service-users with PFI (see 2.7).

Over a one-month period, individuals over the age of 18 were recruited through internal KCL REC research recruitment emails, and through online social media sources including Facebook, Reddit, and/or Twitter, via REC approved advertisements. Individuals were able to respond to advertisements by clicking a link that led them to the study webpage, at their own convenience. The study webpage contained a brief description for the study, and a link to the participant information page, hosted on the Qualtrics platform.

Following the participant information sheet, interested individuals were able to continue to a page to assess eligibility criteria. If participants were not eligible, they were exited from the webpage. Individuals who met eligibility criteria were taken to the consent form, where they were able to provide consent, by selecting a tick box and initialing beside each consent criteria, followed by writing their full name, date and email, and creating a unique identifier code. Participants who provided consent were taken to the baseline questionnaire, which took an average of 34.4 minutes to complete, including reading the information sheet, providing consent, assessing eligibility, and completing the study questionnaire. Three-months following baseline data collection, participants received an email informing them that the 3-month follow-up data collection period was to occur over a two-week period, and included a link to complete the T2 survey, which took an average of 19.3 minutes to complete. Six-months following baseline data collection, participants received an email informing them that the 6-month follow-up data collection period was to occur over a two-week period, and included a link to complete the T3 survey, which took an average of 22.4 minutes to complete.

2.7 Service-User Focus Group

Service-users with PFI were involved in a focus group to provide feedback on the study questionnaire prior to recruitment via an advertisement was posted online on People in Research (<https://www.peopleinresearch.org>). Service-users who responded were invited to read the study information sheet and provide consent to participate in the focus group. Participants were offered £10 for their feedback upon completion of the study questionnaire and feedback survey. Service-users were asked the following questions; (1) did the wording of the questionnaires used make sense to you?; (2) How easy was it for you to understand our survey?; (3) How long did it take you to complete the survey?; (4) Is there anything we did not include on the survey that you think we need to include?; (5) How readable is the font, including size and colour?; (6) Did you have any technical difficulties?; (7) Are there any other comments you would like to provide?.

Six service-users participated in the focus group. Following recommendations, the survey was altered to make the font darker and larger, and a feature was added to enhance continuity of scrolling so that Likert-scale responses were held at the top of the screen for readability. Participants indicated the wording and questionnaires made sense, and indicated they appreciated the inclusion of a 'free text' box at the end of the survey to write anything else about their food intolerance that was not asked. On average, the participants reported the survey took 20 minutes to complete.

2.8 Data Analysis

Qualitative Analysis

Qualitative data was collected to explore the lived experience of PFI and content analysis was used to draw themes from their text (Bengtsson, 2016). Participants were given the option to freely enter text in response to the question *"is there anything else that you would like to tell us about your food intolerance or your experience with food intolerance?"*. The aim was to gather information that may have not been captured through included scales in order to better understand the impact and consequences of PFI in daily life. Further, the hope was to use the qualitative data to complement and provide context to the findings from quantitative analyses if possible. Participant free-text responses were analysed for content, and categories and subcategories were identified (Hsieh & Shannon, 2005) using a deductive (bottom-up) approach, rather than an inductive (top-down) approach in order to illustrate the quantitative findings. The aim of the current study was not to use an inductive approach, though a paper using thematic analyses from semi-structured interviews in a sample of participants (N = 6) from the current study was completed by another student for a separate project.

Statistical Analysis

All statistical analyses were carried out using the statistical software package SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). Analyses were conducted at $\alpha = 0.05$ significance.

Variables were created to assess sample characteristics and outcome measure scores (including sum and subscale scores) at baseline and across T1, T2 and T3. Variables created included age category (18-44 or 45+), identified gender (identifies female or does not identify female), ethnicity (white or BME), PFI characteristics (PFI-only, PFI+FA, severity of PFI, diagnosis of PFI, reported foods and reported symptoms), and additional clinical characteristics (diagnoses of IBS, Coeliac Disease and/or Atopic Disease). Outcome measure scores included illness perceptions (IPQ-R) *including, illness identity, emotional representations, timeline acute/chronic, timeline cyclical, personal control, treatment control, and illness coherence*; coping domains (Brief-COPE) *including self-distraction, active coping, denial, substance use, use of emotional support, use of instrumental support, behavioural disengagement, venting, positive reframing, planning, humour, acceptance, religion, and self-blame*; FR-QoL (SWFL); anxiety (HADS-A); total distress (HADS-T); functional impairment (WSAS); perceived stress (PSS); GI symptom severity (Birmingham IBS-SQ) and extraintestinal symptom severity (PHQ-15). For multivariate analyses, a variable from the PHQ-15 was created which included all but the three items responsible for GI symptoms, to allow for examining GI and extraintestinal symptom severity separately. This new variable to measure extraintestinal symptom severity is referred to as (PHQ).

The data were checked for normality (Appendix V). Univariate and bivariate analyses including average scores, frequencies, independent and paired samples t-tests, chi-square tests for independence, and repeated measures analysis of variance (ANOVAs) were used to calculate sample and clinical characteristics. Bivariate correlation and multivariate regression and mediation analyses were used to explore associations and mediators of 'outcome'. Outcome was measured in two domains across three outcomes; negative affect (including i) anxiety (HADS-A), ii) distress (HADS-Total)) and iii) FR-QoL (SWFL). Previous research supports the use of the HADS-T as a measure of distress (Norton et al., 2013; Norton, Sacker, Young, & Done, 2011), and in the current study the HADS subscales were correlated ($r = .61$), suggesting good concurrent validity. Further, it is important to understand whether there are specific contributing factors that are unique

to anxiety, and additionally that are unique to distress, when HADS-D scores are included in the outcome of “distress”.

Pearson bivariate correlations were conducted to investigate relationships between illness perceptions, coping strategies, and additional psychological and PFI-related factors and outcome. Due to the large number of correlations reported, alpha was set at 0.01 to reduce Type 1 errors. Multivariate analyses including multiple linear regression and mediation were used to explore factors that were associated with outcome and those that mediated outcome (Figure 1 a,b).

Multiple regression analyses (using the forced entry and hierarchical method) were used to examine the total effect of associations of illness perceptions (PH1), coping strategies (PH2) and outcome, and to explore the total effect of additional psychological and PFI-related factors (PH3) and outcome. The regression model is demonstrated in Figure 1a, which illustrates the total effect (c path) of the independent variable (X) on the dependent variable (Y). Preliminary analyses were conducted to ensure no violations of normality, linearity and multicollinearity, Analyses of residuals from the model were performed to assess model fit and check for outliers.

Mediation analysis was conducted using the PROCESS v3.4 (Hayes, 2017) macro for SPSS, to assess direct and indirect mediation effects of illness perceptions, coping responses, and additional factors on outcome. The mediation model is demonstrated in Figure 1b, which illustrates the indirect effects (c' path) of X on Y through a mediating variable (M). A 95% bootstrap-confidence interval (5,000 samples) was used to determine statistical significance.

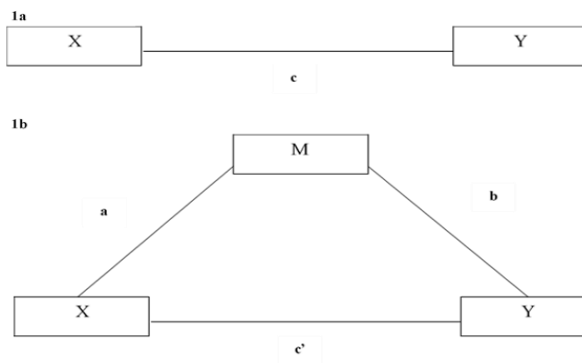


Figure 1. Regression model (1a) and mediation model (1b).

3 Results

3.1 Participant Flow

Recruitment and participation flow information is presented in Figure 2. During the recruitment phase, 349 individuals met criteria and consented to participate in the study.

Baseline data (T1) were collected from (May 22, 2019 until June 5, 2019), and 255 individuals comprised the baseline sample (see Figure 2).

Three-month follow up data (T2) were collected from August 22, 2019 – September 5, 2019. Complete questionnaires were submitted by 170 participants, and following T2, 156 participants completed all T1 and T2 outcome measures (see Figure 2).

Six-month follow-up data (T3) were collected between November 22, 2019 to December 6, 2019. Complete questionnaires were submitted by 110 participants and following T3, matched and complete data at all three time points were obtained for 84 participants (see Figure 2).

Due to the number of participants that were lost to follow up, the decision was made to not include data from T3 in the final mediation model in analysis and will be discussed further in study limitations.

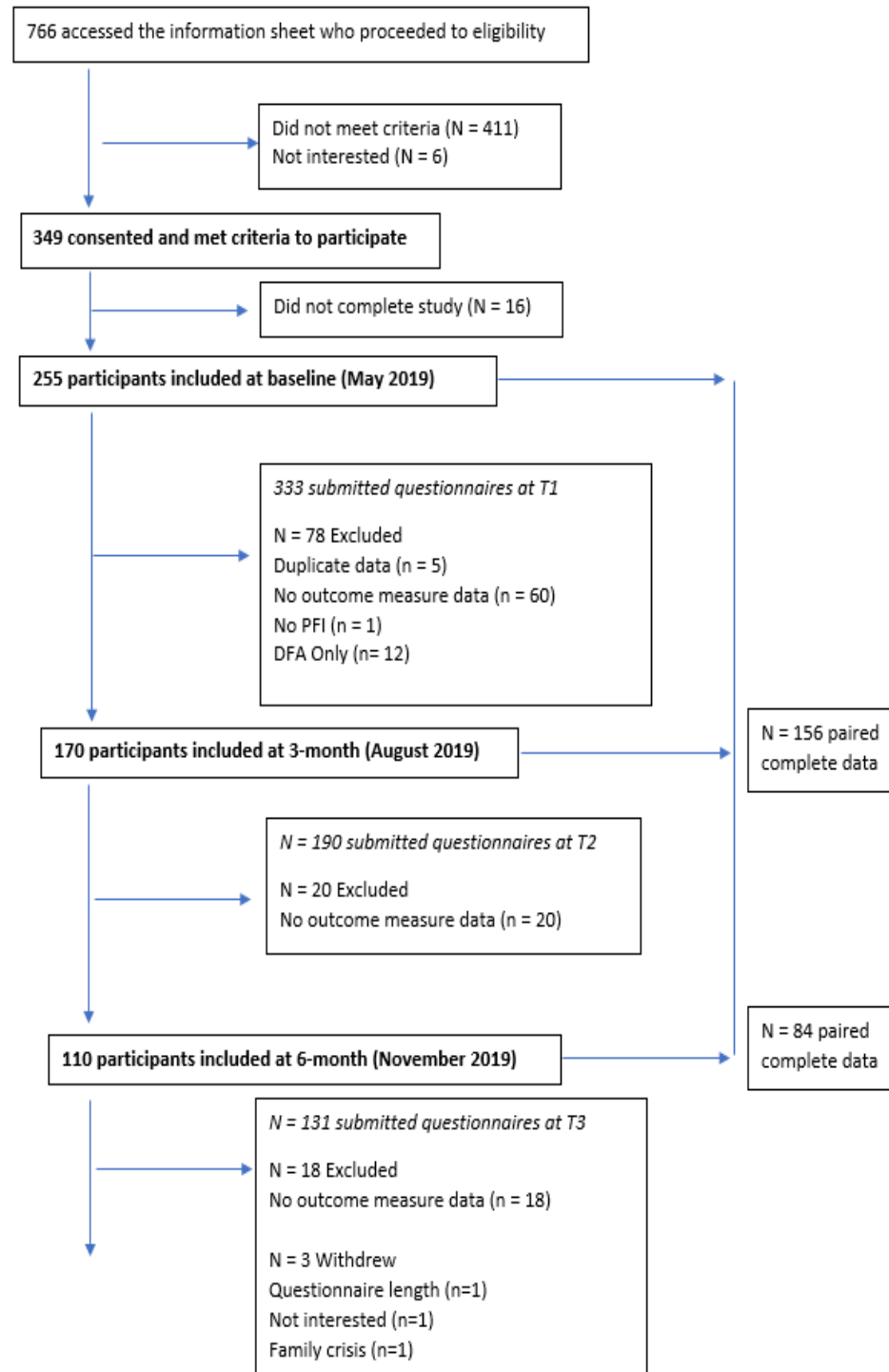


Figure 2. Recruitment and participant flow.

3.2 Presentation of Results

Results are presented following the study hypotheses and aims. Sample characteristics were calculated using univariate descriptive and inferential statistical analyses. To assess PH1, PH2, and PH3 separately and as a whole model, cross-sectional baseline correlations and linear regression analyses were conducted for three outcome variables including anxiety, distress and FR-QoL. To assess primary exploratory aims, paired t-tests and repeated measure ANOVA's were calculated to measure the stability of scores on outcome measures over time (T1 – T2 and T1 – T3) in order to inform subsequent longitudinal mediation analyses. To assess PA1 and PA2, temporally ordered mediation analyses were conducted to identify mediating mechanisms that contribute to outcome, which can aid in developing an effective multifaceted intervention. To assess the secondary exploratory aim, content-analysis was used for the qualitative data.

3.3 Sample Characteristics

At the start of analysis, the sample was split to compare characteristics of individuals who identify female (N = 236; 92.5%) and individuals who do not identify female (N = 19; 7.5%). The significant size difference in these two groups precluded further group analysis, and the results are presented in Appendix VI. The sample was then split to compare characteristics of individuals who self-reported PFI only (N = 194; 76.1%) to individuals who self-reported both PFI and FA (N = 61; 23.9%), and results are presented in Appendix VII. There were no significant demographic differences between groups. PFI-only were more likely to self-report IBS ($\chi^2 = 7.71, p = .006$), and there was a trend for PFI-only to be more likely to self-report Coeliac Disease ($\chi^2 = 3.69, p = .055$). There were no significant differences in baseline scores on outcome measures, or in the proportion of individuals that met HADS subscales caseness threshold.

The sample was split a third time, in order to compare characteristics of participants who reported they had IBS in addition to PFI, against participants who had PFI only. PFI and IBS have considerable demographic and symptom overlap, and it is possible that these groups share other important similarities, or group differences. The results are presented in Appendix VIII. There were no significant differences in identified sex, age, or

ethnicity. A larger proportion of individuals with IBS+ PFI had only PFI and no other identified FA. Furthermore, individuals with IBS were more likely to report intolerance to an increasing number of foods, with 32% of individuals with IBS+PFI reporting intolerance to more than 4 foods. Individuals with IBS + PFI reported significantly increased symptom severity on the IBS-SQ and the PHQ-15, and furthermore, reported significantly increased WSAS scores, indicative of functional impairment, as compared to individuals with PFI only. There were no group differences in anxiety, depression, perceived stress, or FR-QoL, indicating IBS does not further elevate psychological distress.

The study aim was to explore factors in PFI, and all following results are for the sample as a whole. There seem to be important differences between individuals with PFI as compared to individuals with both IBS and PFI, which will be touched on in the discussion. The characteristics of the entire sample are presented in Table 1 & Table 2.

3.3.1 Demographic, PFI-Related and Clinical Characteristics

255 individuals completed T1. The sample ranged from 18 – 74 years, with an average age of 37.7 (15.0), 92.5% identified female, and 90.2% identified Caucasian (Table 1). Age categories were collapsed to examine differences between participants 18-44 and 45+, as has been done previously (see Chapter 1). Information regarding education or employment was not collected and will be discussed under Study Limitations.

The median duration of PFI was 11.6 years, and PFI was primarily self-diagnosed (61.5%). Individuals with PFI reported symptoms in response to more than one food (71.7%) (see Table 1). Additional GI and atopic conditions were reported by participants, including IBS, asthma, environmental allergies and skin-related atopy such as urticaria.

Mean scores (Table 2) on the FR-QoL, WSAS, PHQ-15, and the PSS were within the ‘moderate’ range. No clinical cut-offs are set for the Birmingham IBS-SQ. Mean HADS scores on the depression subscale were below clinical threshold (≥ 8), however, average scores on the HADS-A subscale were above clinical threshold (≥ 8). Across the sample, 59.6% were above clinical cut-off on the HADS-A and considered to meet ‘caseness’ criteria for anxiety.

Table 1
Participant Demographic Characteristics

T1 (N = 255)	
Demographic Characteristics	M (SD) / N (%)
Age	37.7 (15.0)
Identify Female	236 (92.5%)
Caucasian	230 (90.2%)
18-44	162 (63.5%)
PFI & Clinical Characteristics	Mdn [IQR] / N (%)
Duration of PFI	11.6 [9.0–20.5]
PFI Only	194 (76.1%)
PFI & FA	61 (23.9%)
PFI Diagnosis	
Self-Diagnosed	153 (61.5%)
Medical Professional	76 (30.5%)
CAM Practitioner	20 (8.0%)
Number of Offending Foods	
1 food	72 (28.3%)
2 foods	59 (23.5%)
3 foods	55 (21.7%)
4+ foods	67 (26.5%)
Irritable Bowel Syndrome	122 (47.8%)
Coeliac Disease	19 (7.5%)
Atopic Conditions	
Asthma	69 (27.1%)
Skin-Related	63 (24.7%)
Hay-fever/Rhinitis/Allergy	122 (47.8%)
Medication Allergy	66 (25.9%)

Table 2
Participant Outcome Measure Scores

Outcome Measure Scores	T1 (N = 255)	T2 (N = 170)	T3 (N = 110)
	M (SD)	M (SD)	M (SD)
SWFL	23.1 (7.0)	23.8 (7.2)	23.3 (7.7)
HADS Anxiety	9.0 (4.9)	9.0 (5.2)	8.8 (5.7)
HADS Depression	5.9 (4.4)	5.8 (4.5)	5.8 (4.7)
HADS Total	15.0 (8.0)	14.8 (8.7)	14.3 (9.4)
WSAS	10.2 (9.1)	9.1 (9.5)	8.9 (9.0)
PHQ-15	11.7 (5.9)	11.0 (5.5)	10.7 (5.6)
IBS-SQ Sum Score	28.7 (17.4)	26.6 (18.1)	26.6 (18.1)
PSS	20.4 (7.9)	19.6 (8.5)	19.2 (8.8)

3.3.2 Additional PFI Characteristics

Commonly Reported Offending Foods

The most commonly reported intolerance was dairy (including milk and cheese), reported by 57.3% of the sample, followed by gluten and wheat (42.3%) (see Table 3). The 91 and 77 participants who responded that they were intolerant to ‘fruits, vegetables and/or legumes’ and ‘other’ respectively, were asked to indicate which items specifically, and results are displayed in Figure 3 and Figure 4.

Table 3

Commonly Reported Offending Foods

	<i>N</i>	% of sample
Dairy (including milk, cheese and lactose intolerance)	153	57.3%
Gluten and/or Wheat Intolerance	113	42.3%
Fruits, Vegetables, Legumes	91	34.1%
Other	77	28.8%
Egg	40	15%
Nuts and Seeds	34	12.7%
Fructose Intolerance	31	11.6%
Soya	30	11.2%
Shellfish and Seafood	27	10.1%

Commonly Reported Symptoms

GI symptoms including bloating (24%), stomach pain (21%), and constipation or diarrhea (15%), accounted for 60% of reported symptoms. Extraintestinal symptoms including fatigue (10%), mood changes (8%), brain fog (7%), headache (6%), joint pain (6%) and hives/itching skin (3%), comprised 40% of complaints. The foods most frequently reported to cause both GI symptoms and extraintestinal symptoms were dairy, and gluten and/or wheat products.

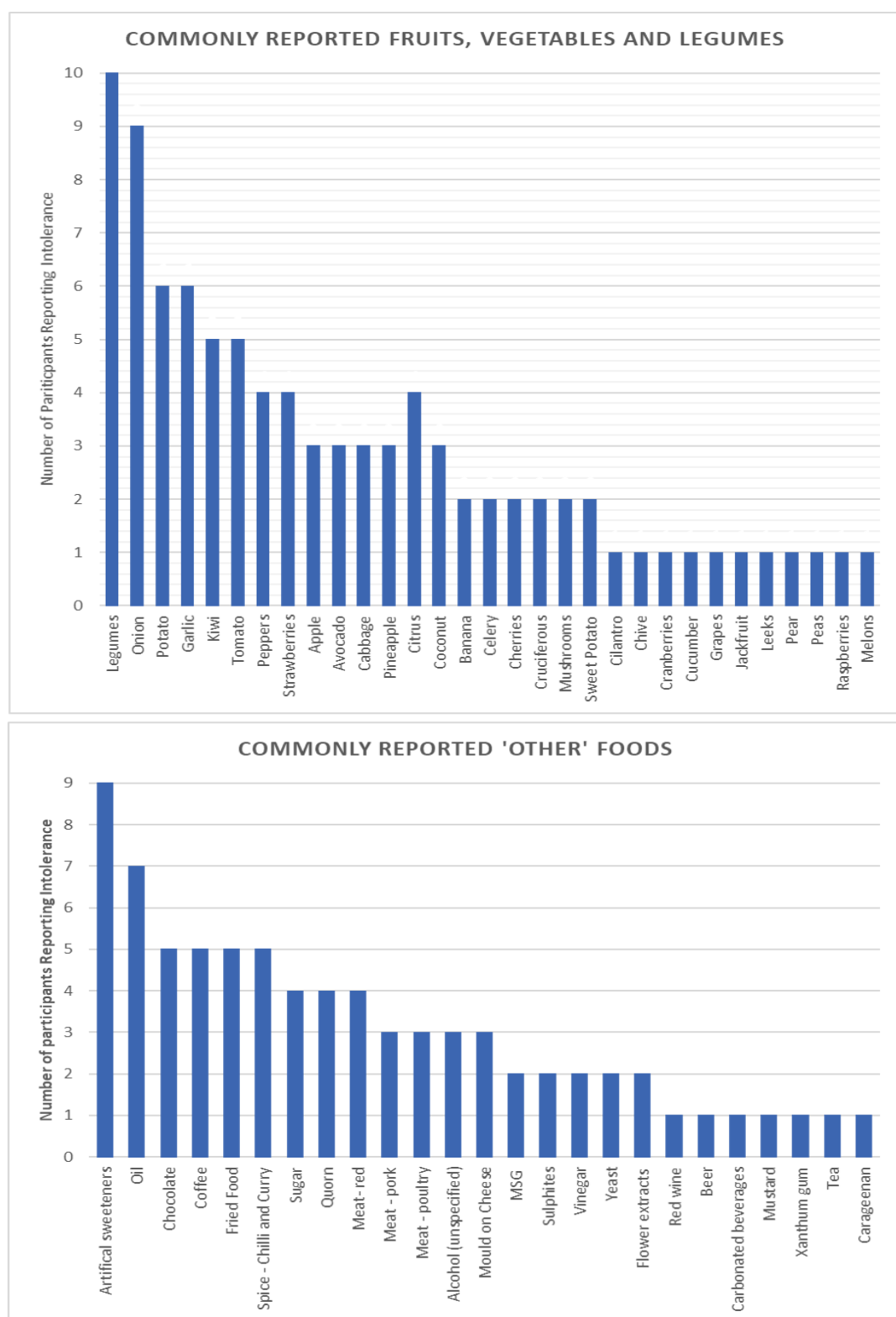


Figure 4. Reported 'other' foods.

Causal Attributions of PFI

The three most endorsed causes of PFI on the IPQ-R were heredity (47.2%), chance/bad luck (46.5%), and diet/eating habits (45.7%) (see Table 4). Psychological attributions were reported by 39.4%. In the free-text section of the IPQ-R participants included their own causal beliefs, and causes relating to gut health, previous health conditions, and medication were frequently described (see Appendix IX).

Table 4

<i>Causal Attributions of PFI</i>		
Cause	N	% of sample
Hereditary	126	47.2%
Chance or bad luck	124	46.5%
Diet or eating habits	122	45.7%
Stress or worry	105	39.4%
My own behaviour	80	30%
Emotional State	76	28.4%
Aging	67	25.1%
Pollution in environment	57	21.4%
Germ or virus	44	16.5%
Poor past medical care	39	14.6%
My mental attitude	39	14.6%
Overwork	37	13.8%
Family problems or worries	34	12.8%
Alcohol	29	10.9%
Smoking	25	9.3%
My Personality	23	8.6%
Altered Immunity	20	7.5%
Accident or Injury	13	4.9%

3.4 Cross-Sectional Results (PH1, PH2): Illness Perceptions, Coping and Outcome

3.4.1 Correlational Analysis

Pearson bivariate correlations were conducted to investigate relationships between illness perceptions, coping strategies and outcome. Only correlations significant at $\alpha = 0.01$ were used. Please refer to Appendix X for the summary correlation matrix.

IPQ-R and HADS-A: Five IPQ-R domains including emotional representations, identity, consequences, cyclical timeline, and illness coherence were significantly associated with anxiety. The strongest correlation was between emotional representations and anxiety ($r = .36$), followed by illness identity ($r = .24$) and cyclical timeline beliefs ($r = .23$). Beliefs about consequences were less strongly correlated to anxiety ($r = .17$). Stronger illness coherence beliefs, representative of an understanding of PFI, was correlated with lower anxiety ($r = -.18$).

IPQ-R & HADS-T: Illness perceptions that were correlated with anxiety were significantly associated with the HADS-T as an outcome of distress. The strongest correlation was between emotional representations and distress ($r = .40$). Illness identity ($r = .27$), consequences ($r = .24$) and cyclical timeline beliefs ($r = .21$) were also associated with distress. Stronger illness coherence was correlated with decreased distress ($r = -.19$).

IPQ-R & SWFL: Four IPQ-R domains correlated with SWFL. The strongest correlation was between consequences and poor SWFL ($r = -.43$), followed by emotional representations ($r = -.41$), illness identity ($r = -.36$), and cyclical timeline beliefs ($r = -.21$).

IPQ-R & Brief COPE: Four Brief-COPE strategies of denial, disengagement, and self-blame were significantly correlated with illness perceptions. Denial was correlated with illness identity ($r = .25$) and emotional representations ($r = .17$). Self-blame was correlated with emotional representations ($r = .22$) and illness identity ($r = .19$). Disengagement was correlated with emotional representations ($r = .29$) and illness identity ($r = .25$) but less strongly correlated with consequences ($r = .21$) and cyclical timeline ($r = .18$). Lower scores on disengagement were correlated with stronger beliefs of personal control ($r = -.19$), treatment control ($r = -.20$) and illness coherence ($r = -.17$).

Brief-COPE & HADS-A: Seven coping responses including self-distraction, denial, substance use, disengagement, venting, positive reframing and self-blame significantly correlated with anxiety. The strongest association was between self-blame and anxiety ($r = .53$), followed by disengagement ($r = .46$) and denial ($r = .33$). Coping responses that

were less correlated with anxiety include self-distraction ($r = .28$), substance use ($r = .19$), and venting ($r = .18$). Positive reframing was the only coping mechanism significantly correlated with decreased anxiety ($r = -.18$).

Brief-COPE & HADS-T: Coping responses that were significantly correlated with anxiety were significantly correlated distress, however, acceptance was additionally correlated. The strongest associations were between self-blame and distress ($r = .56$), followed by disengagement ($r = .56$), and denial ($r = .36$). Coping mechanisms that correlated to a lesser degree include self-distraction ($r = .29$), substance use ($r = .22$), and venting ($r = .20$). Positive reframing ($r = -.22$) and acceptance ($r = -.16$) were correlated with decreased distress. Of note, it appears that once depression is included in the measure of distress, acceptance is associated with lower distress.

Brief-COPE & SWFL: Three coping responses correlated with SWFL. The strongest association was between disengagement and SWFL ($r = -.28$), followed by self-blame ($r = -.27$). Positive reframing was correlated with increased SWFL ($r = .21$).

3.4.2 Multivariate Linear Regression

To assess the strength of associations between IPQ-R and Brief-COPE dimensions and outcome at baseline, multivariate linear regression analyses were conducted using the hierarchical method with factors only significant from correlational analyses.

IPQ-R & COPE on HADS-A as Outcome

Age was included in Step 1 of this model as older age was correlated with decreased anxiety ($r = -.210$). The model explained 42.4% of the variance in anxiety (see Table 5). At Step 1, age contributed significantly $F(1,207) = 9.50$, $p = 0.002$ and accounted for 3.9% of the variation in anxiety. In Step 2, introducing illness perceptions explained an additional 18% of the variance, and this change in R^2 was significant, $\Delta F(5,202) = 10.52$, $p < 0.001$. In Step 3, adding coping domains to the model explained an additional 20.5% of the variation in anxiety and this change in R^2 was significant, $\Delta F(7,195) = 11.36$, $p < 0.001$.

The results showed that illness identity, emotional representations, and coping using self-blame are associated with increased anxiety. Older age and positive reframing are associated with decreased anxiety. The strongest contributor to anxiety in PFI is emotional representations ($\beta = .381$) and self-blame ($\beta = .358$).

Table 5

Cross-Sectional Hierarchical Regression of IPQ-R and Brief-COPE: HADS-A as Outcome

Variable	b	SE b	β	t	p	R	R ²	ΔR^2
Step 1						.209	.039	.044**
Age	-2.275	.683	-.226**	-3.330	.005			
Step 2						.491	.219	.198***
Identity	.430	.117	.254***	3.663	<.001			
Consequences	-.165	.081	-.184	-2.035	ns			
Illness Coherence	-.042	.069	-.043	-.615	ns			
Emotional Rep.	.316	.076	.381***	4.177	<.001			
Timeline Cyclical	.055	.085	.045	.645	ns			
Step 3						.678	.424	.195***
Denial	.428	.268	.105	1.594	ns			
Disengagement	.307	.220	.100	1.400	ns			
Venting	-.200	.212	-.061	-.944	ns			
Positive Reframing	-.406	.158	-.153*	-2.566	.011			
Self-Blame	.855	.173	.358***	4.934	<.001			
Self-Distraction	.126	.186	.044	.677	ns			
Substance Use	-.008	.189	-.003	-.044	ns			

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, ns = nonsignificant, R^2 is adjusted

IPQ-R & COPE on HADS-T as Outcome

The model explained 47% (adjusted R^2) of the variance in distress (see Table 6). At Step 1, illness perceptions explained 18.7% of the variance, and this was significant, $F(5,203) = 10.6$, $p < 0.001$. In Step 2, adding coping domains to the model explained an additional 28.3% of the variation and this change in R^2 was significant, $\Delta F(8,195) = 14.6$, $p < 0.001$. The results revealed that illness identity, emotional representations of PFI, and coping domains of disengagement and self-blame are associated with increased distress, whereas positive reframing is associated with decreased distress. The strongest contributors of increased distress in PFI is strong emotional representations ($\beta = .390$) and a coping response of self-blame ($\beta = .277$).

Table 6*Cross-Sectional Hierarchical Regression of IPQ-R and Brief-COPE: HADS-T as Outcome*

Variable	b	SE b	β	t	p	R	R ²	ΔR^2
Step 1						.454	.187	.206***
Identity	.637	.204	.211**	2.957	.002			
Consequences	-.199	.141	-.130	-1.368	ns			
Illness Coherence	-.121	.120	-.072	-.977	ns			
Emotional Rep.	.552	.131	.390***	4.086	<.001			
Timeline Cyclical	.019	.147	.009	.136	ns			
Step 2						.709	.470	.297***
Acceptance	-.483	.283	-.099	-1.706	ns			
Denial	.725	.443	.104	1.635	ns			
Disengagement	1.30	.358	.248***	3.634	<.001			
Venting	-.435	.343	-.078	-1.271	ns			
Positive Reframing	-.593	.277	-.131*	-2.142	.033			
Self-Blame	1.127	.284	.277***	3.974	<.001			
Self-Distraction	.477	.303	.099	1.573	ns			
Substance Use	-.033	.311	-.006	-.106	ns			

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, ns = nonsignificant, R^2 is adjusted*IPQ-R & COPE on SWFL as Outcome*

The model explained 26.7% of the variance in poor FR-QoL (see Table 7). In Step 1, illness perceptions explained 22.3%, and this was significant, $F(4,206) = 16.08$, $p < 0.001$. In Step 2, coping domains explained an additional 4.4% of the variation in poor FR-QoL and this change in R^2 was significant, $\Delta F(3,203) = 5.15$, $p = 0.002$. The results imply that illness identity and emotional representations of PFI are associated with poorer FR-QoL, whereas positive reframing is associated with improved FR-QoL. The strongest contributor of poor FR-QoL are strong emotional representations of PFI ($\beta = -.214$).

Table 7*Cross-Sectional Hierarchical Regression of IPQ-R and Brief-COPE: SWFL as Outcome*

Variable	b	SE b	β	t	p	R	R ²	ΔR^2
Step 1						.488	.223	.238***
Identity	-.409	.163	-.173**	-2.513	.013			
Consequences	-.203	.113	-.162	-1.804	ns			
Emotional Rep.	-.247	.102	-.214**	-2.426	.016			
Timeline Cyclical	-.177	.111	-.104	-1.588	ns			
Step 2						.540	.267	.054**
Disengagement	-.107	.327	-.025	-.328	ns			
Positive Reframing	.665	.225	.179**	2.954	.004			
Self-Blame	-.443	.244	-.132	-1.818	ns			

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, ns = nonsignificant, R^2 is adjusted

3.5 Cross-Sectional Results (PH3): Additional Psychological and PFI-related Factors on Outcome

3.5.1 Correlational Analyses

Pearson bivariate correlation coefficients were conducted to investigate relationships between additional factors and outcome (refer to Appendix XI for the correlation matrix). Only correlations significant at $\alpha = 0.01$ are reported.

HADS-A: Elevated anxiety was significantly correlated with increased scores of scales of perceived stress (PSS), ($r = 0.70$), extraintestinal symptom severity (PHQ) ($r = .56$), GI symptom severity (IBS-SQ) ($r = .38$), functional impairment (WSAS), ($r = .36$), poorer FR-QoL (SWFL) ($r = -.33$), and increased severity of PFI ($r = .18$).

HADS-T: Elevated distress was significantly correlated with increased scores of stress ($r = .76$), extraintestinal symptoms ($r = .59$), GI symptoms ($r = .38$) functional impairment ($r = .47$), poorer FR-QoL ($r = -.39$).

SWFL: Poor FR-QoL was significantly correlated with scores of increased anxiety (HADS-A) ($r = -.33$), distress (HADS-T) ($r = -.39$), perceived stress ($r = -.42$), extraintestinal symptoms ($r = -.41$), GI symptoms ($r = -.43$), functional impairment ($r = -.39$), and increased severity of PFI ($r = -.32$).

3.5.2 Multivariate Linear Regression

Hierarchical multivariate linear regression was used to assess the strength of associations between additional psychological and PFI-related factors and outcome at baseline, only using factors significant from correlational analyses. In the anxiety and distress models, the PSS score was entered separately to control for its effects, as stress, anxiety and distress are highly correlated.

HADS-A as Outcome

The model explained 54.2% of the variance in anxiety (see Table 8). Age was entered to control for its effect at Step 1, and contributed significantly to the model, $F(1,210) = 10.52$, $p = 0.001$, accounting for 4.3% of the variance. In Step 2, PSS scores explained an additional 43.9% and this change in R^2 was significant, $\Delta F(1,209) = 179.14$, $p < 0.001$. In Step 3, additional factors and PFI severity explained a further 6% of the variance, and this change in R^2 was significant, $\Delta F(5,204) = 6.48$, $p < 0.001$. Increased stress (PSS) and extraintestinal symptom severity (PHQ) are associated with elevated anxiety, whereas older age is associated with decreased anxiety. Apart from stress, the strongest contributor to elevated anxiety are extraintestinal symptoms ($\beta = .279$).

Table 8

Cross-Sectional Hierarchical Regression of Additional Factors Associated with PFI: HADS-A as Outcome

Variable	b	SE b	β	t	p	R	R ²	ΔR^2
Step 1						.218	.043	.048***
Age	-2.180	.672	-.229***	-3.273	.001			
Step 2						.698	.482	.440***
PSS	.419	.033	.675***	12.754	<.001			
Step 3						.747	.542	.070***
SWFL	-.018	.040	-.025	-.450	ns			
WSAS	.022	.029	.046	.773	ns			
PHQ	.238	.060	.279***	3.964	<.001			
IBS-SQ	-.006	.018	.022	.344	ns			
PFI Severity	.062	.153	.021	.404	ns			

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, ns = nonsignificant, R^2 is adjusted

HADS-T as Outcome

The model explained 63.2% of the variance in distress (see Table 9). At Step 1, PSS scores explained 55.7% of variation in distress, $F(1,213) = 270.20$, $p < 0.001$. In Step 2, introducing outcome measures explained a further 7.5% of the variance, and this change in R^2 was significant, $\Delta F(4,209) = 11.99$, $p < 0.001$. The results indicate that increased stress (PSS), extraintestinal symptom severity (PHQ), and functional impairment (WSAS) are significantly associated with distress. Apart from stress, the strongest contributor to elevated distress are extraintestinal symptoms ($\beta = .268$).

Table 9*Cross-Sectional Hierarchical Regression of Additional Factors Associated With PFI: HADS-T as Outcome*

Variable	b	SE b	β	t	p	R	R ²	ΔR^2
Step 1						.748	.557	.589***
PSS	.788	.047	.748***	16.438	<.001			
Step 2						.801	.632	.082***
SWFL	-.040	.053	-.033	-.671	ns			
WSAS	.116	.042	.142**	2.756	.006			
PHQ	.384	.089	.268***	4.306	<.001			
IBS-SQ	-.031	.027	-.065	-1.144	ns			

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, ns = nonsignificant, R^2 is adjusted*SWFL as Outcome*

The model explained 27.8% of the variance in poor FR-QoL (see Table 10), $F(7,203) = 12.55$, $p < 0.001$. Increased stress (PSS), increased GI symptom severity (IBS-SQ), and increased severity of PFI, indicated by a greater number of offending foods are significantly associated with poorer FR-QoL. Perceived stress was the strongest contributor to poor FR-QoL ($\beta = -.229$)

Table 10*Cross-Sectional Hierarchical Regression of Additional Factors Associated with PFI: SWFL As Outcome*

Variable	b	SE b	β	t	p	R	R ²	ΔR^2
						.550	.278	.302***
HADS-A	.009	.128	.006	.072	ns			
HADS-D	-.188	.139	-.117	-1.347	ns			
WSAS	-.076	.051	-.113	-1.481	ns			
PHQ	.042	.111	.035	.374	ns			
PSS	-.201	.077	-.229**	-2.610	.010			
IBS-SQ	-.082	.032	-.203**	-2.590	.010			
PFI Severity	-.793	.269	-.190**	-2.950	.004			

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, ns = nonsignificant, R^2 is adjusted

3.6 Cross-sectional Results (PH1 +PH2 +PH3): Illness Perceptions, Coping and Additional Factors on Outcome

Results from the cross-sectional regression analyses revealed specific illness perceptions, coping and additional factors associated with anxiety, distress and FR-QoL. To explore the impact of illness perceptions (PH1) and coping responses (PH2) on outcome while controlling for additional factors (PH3), complete hierarchical regression

models were analysed using variables that were significant from previous regressions. In the anxiety and distress models, PSS was not entered, as stress, anxiety and distress are highly correlated. All R^2 reported are adjusted.

HADS-A as Outcome

The model explained 46.3% of the variance in anxiety (see Table 11). At Step 1, age was entered to control for its effect, and contributed significantly to the model $F(1,212) = 10.24$, $p < 0.01$, accounting for 4.2% of the variance. In Step 2, PHQ scores explained an additional 28.5% of variation in anxiety and this change in R^2 was significant, $\Delta F(1,211) = 90.70$, $p < 0.001$. In Step 3, illness perceptions explained a further 1.8% of the variance, and this change in R^2 was significant, $\Delta F(2,209) = 4.16$, $p < 0.05$. In Step 4, coping responses explained an additional 11.8% of the variance, and this change in R^2 was significant, $\Delta F(2,207) = 24.06$, $p < 0.001$. Increased severity of extraintestinal symptoms (PHQ), emotional representations and self-blame are associated with elevated anxiety, whereas older age and positive reframing are associated with decreased anxiety. The strongest contributors to increased anxiety are extraintestinal symptoms ($\beta = .542$) and a coping response of self-blame ($\beta = .345$).

Table 11

Cross-Sectional Hierarchical Regression of Additional Factors, IPQ-R, And Brief-COPE: HADS-A as Outcome

Variable	b	SE b	β	t	p	R	R^2	ΔR^2
Step 1						.215	.042	.046**
Age	-2.169	.678	-.215**	-3.200	.002			
Step 2						.577	.327	.287***
PHQ	.452	.047	.542***	9.52	<.001			
Step 3						.598	.345	.024*
Illness Identity	.004	.113	.002	.031	ns			
Emotional Rep.	.144	.052	.174**	2.797	.006			
Step 4						.691	.463	.121***
Self-Blame	.828	.134	.345***	6.188	<.001			
Positive Reframing	-.394	.135	-.148**	-2.910	.004			

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, ns = nonsignificant, R^2 is adjusted

HADS-T as Outcome

The model explained 53.4% of the variance in distress (see Table 12). At Step 1, increased PHQ and WSAS scores were significant contributors, $F(2,209) = 69.78$, $p < 0.001$, accounting for 39.5% of the variance. In Step 2, illness perceptions explained only 0.4% of the variance, and this was not significant, $\Delta F(2,207) = 1.87$, $p = 0.170$. In Step 3, coping responses explained an additional 13.5% of the variance, and this change in R^2 was significant, $\Delta F(3,204) = 20.94$, $p < 0.001$. The results suggest that increased severity of extraintestinal symptoms (PHQ), functional impairment (WSAS), and coping responses of self-blame and disengagement are associated with elevated distress, whereas positive reframing is associated with decreased distress. The strongest contributors to distress are extraintestinal symptom severity ($\beta = .410$) and self-blame ($\beta = .268$).

Table 12

Cross-Sectional Hierarchical Regression of Additional Factors, IPQ-R, And Brief-COPE: HADS-T as Outcome

Variable	b	SE b	β	t	p	R	R ²	ΔR^2
Step 1						.633	.395	.400***
PHQ	.579	.093	.410***	6.236	<.001			
WSAS	.248	.054	.300***	4.564	<.001			
Step 2						.641	.399	.010
Illness Identity	-.211	.184	-.074	-1.150	ns			
Emotional Rep.	.141	.090	.100	1.571	ns			
Step 3						.741	.534	.139***
Self-Blame	1.091	.240	.268***	4.550	<.001			
Positive Reframing	-.625	.218	-.139**	-2.869	.005			
Disengagement	.897	.334	.171**	2.686	.008			

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, ns = nonsignificant, R^2 is adjusted

SWFL as Outcome

The model explained 32.6% of the variance in FR-QoL (see Table 13). At Step 1 increased PSS and IBS scores, and PFI severity contributed significantly to the model, $F(3,202) = 37.31$, $p < 0.001$, accounting for 27.8% of the variance. In Step 2, illness perceptions explained a further 3.3% of the variance, and this change in R^2 was significant, $\Delta F(2,200) = 5.68$, $p < 0.05$. In Step 3, coping responses explained an additional 1.5% of the variance, and this change in R^2 was significant, $\Delta F(1,199) = 5.44$, $p < 0.05$. The results indicate stress (PSS), severity of GI symptoms (IBS-SQ), PFI severity, illness identity, and emotional representations are associated with poor FR-QoL, whereas positive reframing

is associated with improved FR-QoL. The strongest contributors to FR-QoL are stress ($\beta = -.328$) and GI symptom severity ($\beta = -.233$).

Table 13

Cross-Sectional Hierarchical Regression of Additional Factors, IPQ-R, And Brief-COPE: SWFL as Outcome

Variable	b	SE b	β	t	p	R	R ²	ΔR^2
Step 1						.537	.278	.289***
PSS	-.280	.054	-.328***	-5.231	<.001			
IBS-SQ	-.093	.026	-.233***	-3.532	<.001			
PFI Severity	-.784	.258	-.191**	-3.035	.003			
Step 2						.572	.311	.039**
Illness Identity	-.315	.156	-.130*	-2.017	.045			
Emotional Rep.	-.190	.078	-.165*	-2.436	.016			
Step 3						.588	.326	.018*
Positive Reframing	.521	.223	.139*	2.333	.021			

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, R^2 is adjusted

3.7 Longitudinal Results (PA1, PA2): Change Scores and Mediation Analyses

3.7.1 Change in Scores Over Time

Change scores were calculated to assess the stability of illness perceptions, coping strategies, and additional factors over time. All IPQ-R, Brief-COPE, and additional psychological factors were used in change score analyses, but only the IPQ-R and Brief-COPE factors clinically significant from regression analyses are shown in Table 14. Paired samples t-tests were used to examine the difference in scores between T1 – T2, and a repeated measures ANOVA was used to examine change scores between T1 – T3. Results determined no significant differences in IPQ-R, Brief- COPE, or additional outcome measure scores from T1 – T2, or from T1 – T3. These findings demonstrate the relative stability of PFI and impact of PFI over time, of illness perceptions related to PFI and use of coping strategies over time.

Table 14*Paired Mean Scores at T1, T2 and T3 and Change Score Statistics*

Variable	T1 (N = 255)	T2 (N = 170)	Change in scores T1 – T2	T3 (N = 110)	Change in scores T1 – T3
	<i>M(SD)</i>	<i>M(SD)</i>	<i>T-Statistic</i>	<i>M(SD)</i>	<i>F-Statistic</i>
SWFL	23.2 (7.0)	23.8 (7.2)	$t(149) = 0.49, p > .05$	23.7 (7.1)	$F(2, 158) = 0.06, p > .05$
HADS-A	9.0 (4.9)	9.00 (5.2)	$t(140) = -0.77, p > .05$	9.0 (5.6)	$F(1.8, 135.6) = 1.18, p > .05$
HADS-D	6.0 (4.4)	5.8 (4.5)	$t(140) = -1.17, p > .05$	5.7 (4.6)	$F(2, 150) = 0.56, p > .05$
HADS-T	15.0 (8.5)	14.8 (8.7)	$t(140) = -1.13, p > .05$	14.8 (9.2)	$F(2, 150) = 1.09, p > .05$
WSAS	10.4 (10.5)	9.1 (9.5)	$t(138) = -0.93, p > .05$	8.9 (9.0)	$F(1.8, 133.6) = 1.71, p > .05$
PHQ	11.8 (5.9)	11.0 (5.5)	$t(138) = -0.90, p > .05$	10.7 (5.6)	$F(1.8, 130.5) = 1.48, p > .05$
IBS Total	28.8 (17.4)	26.6 (18.1)	$t(133) = 0.24, p > .05$	26.0 (19.1)	$F(1.8, 130.2) = 0.60, p > .05$
PSS	20.4 (7.9)	19.6 (8.5)	$t(135) = 0.70, p > .05$	19.1 (8.6)	$F(1.8, 124.7) = 0.20, p > .05$
Illness Identity	4.4 (3.0)	4.0 (3.0)	$t(140) = 0.81, p > .05$	4.2 (3.0)	$F(2, 152) = 2.79, p > .05$
Emotional Rep.	16.3 (6.0)	16.1 (6.1)	$t(153) = -1.09, p > .05$	16.1 (6.0)	$F(2, 166) = 0.00, p > .05$
Disengage.	3.3 (1.6)	3.3 (1.7)	$t(133) = -0.81, p > .05$	3.0 (1.5)	$F(2, 150) = 0.56, p > .05$
Self-blame	4.3 (2.1)	4.2 (2.0)	$t(135) = 0.61, p > .05$	3.8 (1.9)	$F(1.6, 116.0) = 1.18, p > .05$
Positive Reframing	4.0 (1.8)	4.0 (1.7)	$t(134) = 0.69, p > .05$	4.0 (1.8)	$F(2, 142) = 0.09, p > .05$

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Note: mean scores described in Table 14 are paired means only, as these provide the basis for subsequent analyses, not the whole-sample means described in Table 1.

3.7.2 Mediation Analysis

Temporally ordered mediation analyses were carried out to determine the direct and indirect effects of illness perceptions, coping responses, and additional psychological and PFI-related factors at T1 on outcome at T2, using factors significantly related from regression analyses. Models were tested using bootstrapping, which determines indirect effect sizes and additionally produces a bias-corrected bootstrap (BCB) 95% confidence interval. An indirect effect is assumed to be significant if the BCB confidence interval does not include zero (Hayes, 2009). Due to considerable attrition from T1 – T3, T2 outcome scores at T2 were used in mediation analyses.

3.7.2.1 Illness Perceptions, Coping and Outcome (PA1)

To test the suitability of the CSM, mediation analyses were conducted to explore the mediating effects of coping on outcome (see Figure 5). See Appendix XII for figures for non-significant models.

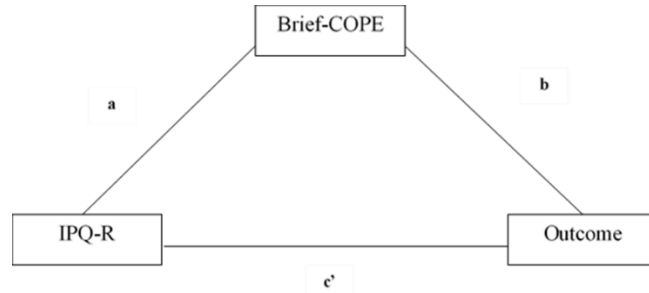


Figure 5. *IPQ-R, Brief-COPE and outcome mediation model*

HADS-A as Outcome

Four models were tested to explore the direct and indirect effects of illness identity, emotional representations, positive reframing, and self-blame on anxiety. The results are presented in Table 15, and Figure 6 shows the full (6a) and partial (6b) mediation models. Positive reframing was not a significant mediator of anxiety (see Appendix XII). Self-blame completely mediated the effects of illness identity ($b = .27$) Figure 6a, and partially mediated the effects of emotional representations ($b = .21$) Figure

6b, on anxiety. Examining path effect sizes revealed that self-blame had a stronger influence on anxiety (b path) than the total effect of illness perceptions (C path).

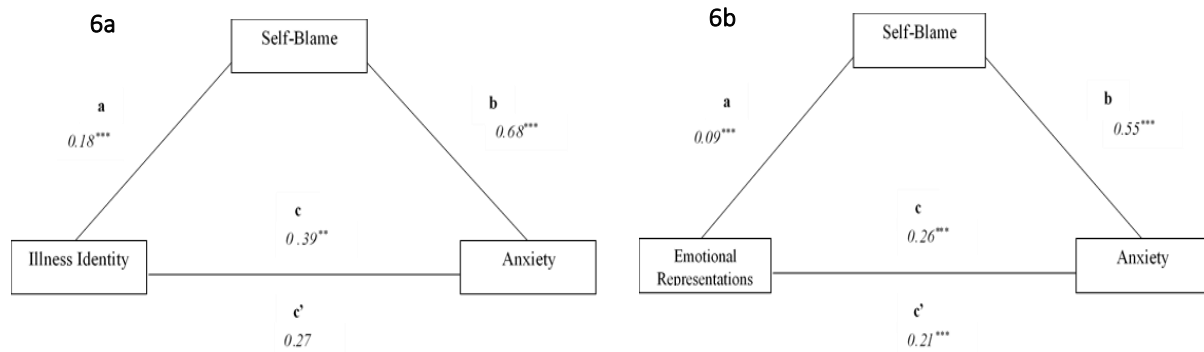


Figure 6. IPQ-R, Brief-COPE and HADS-A significant mediation models

HADS-T as Outcome

Six models (see Table 15) investigating distress as an outcome were tested to explore the direct and indirect effects of illness identity, emotional representations, positive reframing, self-blame, and disengagement. Figure 7(a,b,c) presents the partial mediation models. Positive reframing was not a significant mediator (see Appendix XII). Self-blame (Figure 7(a,b)) partially mediated the effects of illness identity ($b = .58$) and

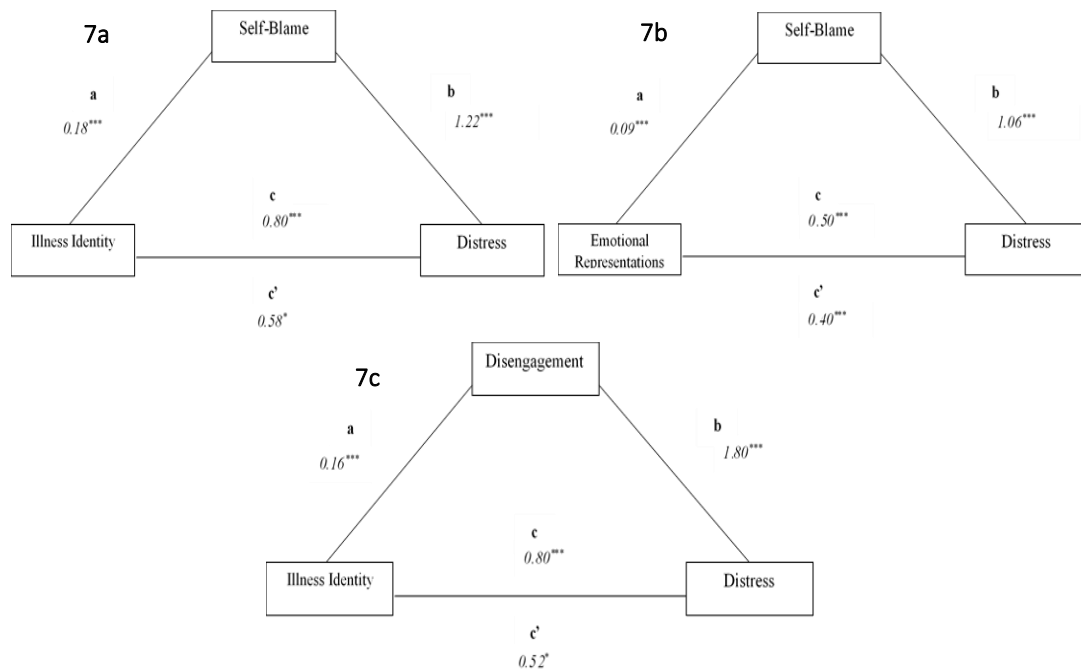


Figure 7. IPQ-R, Brief-COPE and HADS-T significant mediation models

emotional representations ($b = .40$), and disengagement (Figure 7c) partially mediated the effects of illness identity ($b = .52$). Path effect sizes demonstrate that self-blame and disengagement had a stronger influence on distress than the total effect of illness perceptions.

SWFL as Outcome

Two models examining FR-QoL as an outcome were tested to investigate the direct and indirect effects of illness identity, emotional representations and positive reframing (see Table 15). There was no significant indirect effect of illness perceptions on FR-QoL through coping (see Appendix XII). Examining path effect sizes revealed that illness perceptions had a stronger influence on FR-QoL than coping domains.

3.7.2.2 Additional Factors, Coping and Outcome (PA2)

Mediation analyses explored possible mediating roles of additional factors, coping (negative affect models) and illness perceptions (FR-QoL models) on outcome. Figures for not significant models can be found in Appendix XIII.

HADS-A as Outcome

Two models were tested to explore the direct and indirect effects of extraintestinal symptom severity (PHQ) and coping responses of self-blame and positive reframing on anxiety. The results are presented in Table 16. Coping responses did not mediate the effect of extraintestinal symptoms on anxiety (see Appendix XIII).

HADS-T as Outcome

Seven models were tested to explore the direct and indirect effects of extraintestinal symptom severity (PHQ) and functional impairment (WSAS), coping responses of self-blame, positive reframing, and disengagement on distress. The results are presented in Table 16, and Figure 8 shows the partial (8 a,b) and full (8c) mediation models. Positive reframing was not a significant mediator in any model tested, and coping

strategies were not significant mediators of extraintestinal symptoms (see Appendix XIII). Self-blame ($b = .27$) and disengagement ($b = .29$) partially mediated the effects of functional impairment (Figure 8a, and 9b, respectively). Extraintestinal symptom severity fully mediated (Figure 9c) the effect of functional impairment on distress ($b = .06$).

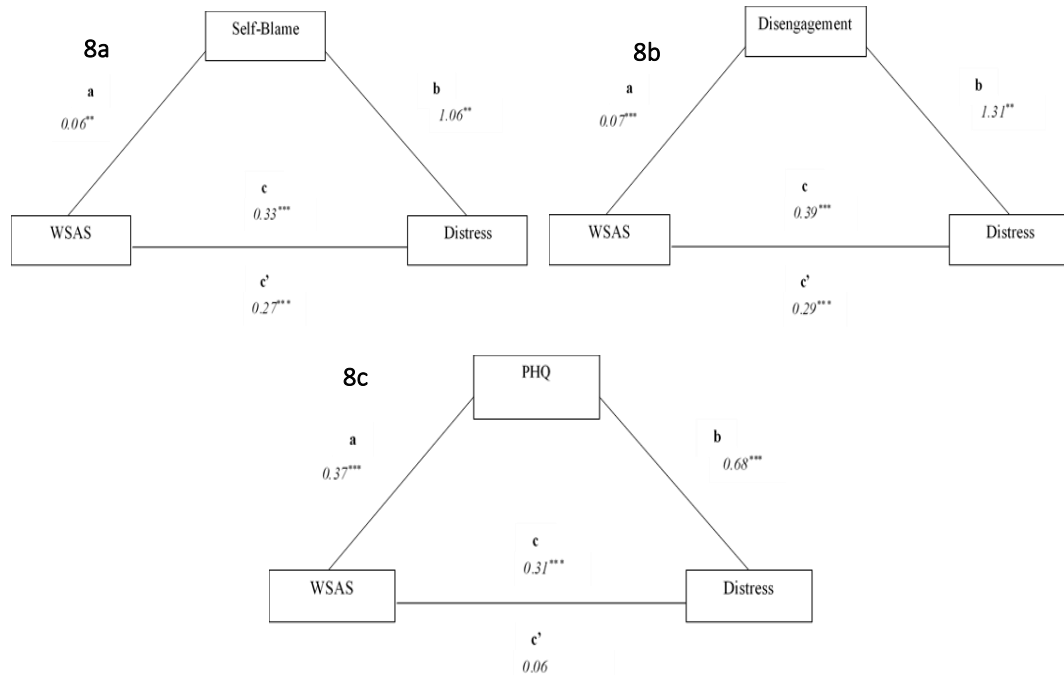


Figure 8. Additional factors and HADS-T significant mediation models

SWFL as Outcome

Seven models were tested to explore whether stress, GI symptom severity, and PFI severity directly impacted FR-QoL, or whether illness identity and emotional representations mediated this, and additionally to explore whether GI symptom severity mediated the effect of stress in FR-QoL. The results are presented in Table 16, and Figure 9 shows the and partial (9 a,b,c,d) and full (9 e,f) mediation models. Figures for non-significant models can be found in Appendix XIII. A stronger illness identity of PFI partially mediated the effects of increased stress ($b = -.27$) on FR-QoL (Figure 9a). Emotional representations of PFI partially mediated the effects of stress ($b = -.18$) and GI symptom severity ($b = -.16$) on FR-QoL (Figure 9 b, c). Increased GI symptom severity partially mediated the effect of stress ($b = -.15$), Figure 9d. The effects of increased PFI severity

(Figure 9e,f) were fully mediated by illness identity ($b = -.40$) and emotional representations of PFI ($b = -.30$).

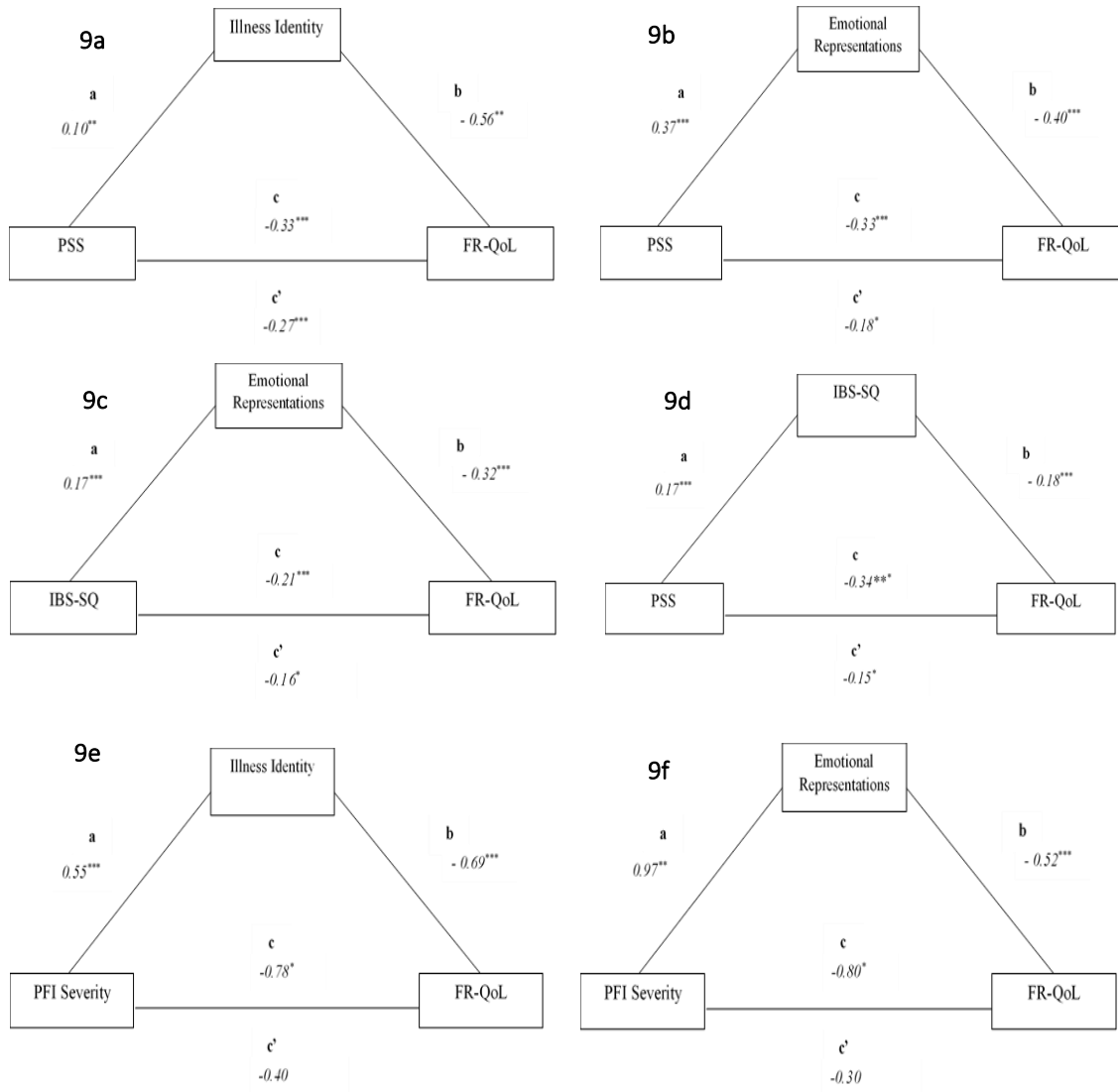


Figure 9. Additional factors and SWFL significant mediation models

Table 15

Mediation Results Summary: IPQ-R, Brief-COPE and Outcome

X <i>Illness Perceptions</i>	Path a X → M	M <i>Coping</i>	Path b M → Y	Y <i>Outcome</i>	Path c' X → M → Y	Path C X → Y	Indirect Effect (95%BCBCI*)
Illness Identity	$b = .18^{***}$ $p < .001$	Self-Blame	$b = .68^{***}$ $p < .001$	Anxiety	$\diamond b = .27$ $p = ns$	$b = .39^{***}$ $p < .001$	$b = .12$ (.03, .25)
Illness Identity	$b = -.01$ $p = ns$	Pos. Reframe	$b = -.31$ $p = ns$	Anxiety	$b = .39^{***}$ $p < .001$	$b = .40^{***}$ $p < .001$	$b = .00$ (-.04 - .05)
Emotional Rep.	$b = .09^{***}$ $p < .001$	Self-Blame	$b = .55^{**}$ $p = .01$	Anxiety	$\diamond b = .21^{***}$ $p < .001$	$b = .26^{***}$ $p < .001$	$b = .05$ (.01, .11)
Emotional Rep.	$b = -.03$ $p = ns$	Pos. Reframe	$b = -.24$ $p = ns$	Anxiety	$b = .26^{***}$ $p < .001$	$b = .27^{***}$ $p < .001$	$b = .01$ (-.01, .03)
Illness Identity	$b = .18^{***}$ $p < .001$	Self-Blame	$b = 1.22^{***}$ $p < .001$	Distress	$\diamond b = .58^*$ $p = .02$	$b = .80^{***}$ $p < .001$	$b = .22$ (.05, .42)
Illness Identity	$b = -.01$ $p = ns$	Pos. Reframe	$b = -.89^*$ $p = .02$	Distress	$b = .81^{***}$ $p < .001$	$b = .81^{***}$ $p < .001$	$b = .01$ (- .11, .13)
Illness Identity	$b = .16^{***}$ $p < .001$	Disengag ement	$b = 1.80^{***}$ $p < .001$	Distress	$\diamond b = .52^*$ $p = .04$	$b = .80^{***}$ $p < .001$	$b = .28$ (.07, .54)
Emotional Rep.	$b = .09^{***}$ $p < .001$	Self-Blame	$b = 1.06^{***}$ $p < .001$	Distress	$\diamond b = .40^{***}$ $p < .001$	$b = .50^{***}$ $p < .001$	$b = .10$ (.02, .20)
Emotional Rep.	$b = -.03$ $p = ns$	Pos. Reframe	$b = -.73^*$ $p = .04$	Distress	$b = .48^{***}$ $p < .001$	$b = .50^{***}$ $p < .001$	$b = .02$ (-.02, .08)
Emotional Rep.	$b = .00$ $p = ns$	Disengag ement	$b = 2.82^{***}$ $p < .001$	Distress	$b = .50^{***}$ $p < .001$	$b = .49^{***}$ $p < .001$	$b = -.01$ (-.17, .18)
Illness Identity	$b = .00$ $p = ns$	Pos. Reframe	$b = .69^*$ $p = .02$	Fr-QoL	$b = -.77^{***}$ $p < .001$	$b = -.77^{***}$ $p < .001$	$b = .00$ (-.09, .09)
Emotional Rep.	$b = -.04$ $p = ns$	Pos. Reframe	$b = .47$ $p = ns$	FR-QoL	$b = -.48^{***}$ $p < .001$	$b = -.50^{***}$ $p < .001$	$b = -.02$ (-.06, .01)

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, BCB-CI* = bias-corrected bootstrap confidence intervals, \diamond denotes partial mediation in the c' path, $\diamond\diamond$ denotes full mediation in the c' path.

Table 16

Mediation Results Summary: Additional Factors, IPQ-R, Brief-COPE and Outcome

X Additional Factors	Path a X → M	M Coping or IPQ-R	Path b M → Y	Y Outcome	Path c' X → M → Y	Path C X → Y	Indirect Effect (95%BCBCI*)
PHQ	$b = .16^{***}$ $p < .001$	Self-Blame	$b = .26$ $p = .22$	Anxiety	$b = .33^{***}$ $p < .001$	$b = .37^{***}$ p $< .001$	$b = .04$ (-.02, .12)
PHQ	$b = -.001$ $p = .862$	Pos. Reframe	$b = -.31$ $p = .12$	Anxiety	$b = .37^{***}$ p $< .001$	$b = .37^{***}$ p $< .001$	$b = .00$ (-.02, .02)
PHQ	$b = .16^{***}$ $p < .001$	Self-Blame	$b = .41$ $p = .23$	Distress	$b = .68^{***}$ p $< .001$	$b = .74^{***}$ p $< .001$	$b = .07$ (-.03, .19)
PHQ	$b = -.001$ $p = .863$	Pos. Reframe	$b = -.87^{**}$ $p = .006$	Distress	$b = .74^{***}$ $p < .001$	$b = .75^{***}$ p $< .001$	$b = .00$ (-.04, .04)
PHQ	$b = .12^{***}$ $p < .001$	Disengag.	$b = .73$ $p = .12$	Distress	$b = .65^{***}$ p $< .001$	$b = .74^{***}$ p $< .001$	$b = .09$ (-.03, .23)
WSAS	$b = .06^{**}$ $p = .002$	Self-Blame	$b = 1.06^{**}$ $p = .002$	Distress	$b = .27^{***}$ $p < .001$	$b = .33^{***}$ p $< .001$	$b = .06$ (.01, .13)
WSAS	$b = -.01$ $p = ns$	Pos. Reframe	$b = -.79^*$ $p = .02$	Distress	$b = .35^{***}$ p $< .001$	$b = .36^{***}$ p $< .001$	$b = .01$ (-.02, .05)
WSAS	$b = .07^{***}$ $p < .001$	Disengage	$b = 1.31^{**}$ $p = .01$	Distress	$b = .29^{***}$ $p < .001$	$b = .39^{***}$ p $< .001$	$b = .09$ (.02, .20)
WSAS	$b = .37^{***}$ $p < .001$	PHQ	$b = .68^{***}$ $p < .001$	Distress	$b = .06$ $p = .46$	$b = .31^{***}$ $p < .001$	$b = .25$ (.13, .40)
PSS	$b = .10^{**}$ $p = .003$	Illness Identity	$b = -.56^{**}$ $p = .004$	Fr-QoL	$b = -.27^{***}$ $p < .001$	$b = -.33^{***}$ $p < .001$	$b = -.05$ (-.12, -.01)
PSS	$b = .37^{***}$ $p < .001$	Emotional Repres.	$b = -.40^{***}$ $p < .001$	FR-QoL	$b = -.18^*$ $p = .02$	$b = -.33^{***}$ $p < .001$	$b = -.15$ (-.25, -.07)
PSS	$b = .17^{***}$ $p < .001$	IBS-SQ	$b = -.18^{***}$ $p < .001$	FR-QoL	$b = -.15^*$ $p = .04$	$b = -.34^{***}$ $p < .001$	$b = -.18^{***}$ (-.27, -.10)
IBS-SQ	$b = .07^{***}$ $p < .001$	Illness Identity	$b = -.41^*$ $p = .04$	FR-QoL	$b = -.18^{***}$ $p < .001$	$b = .21^{***}$ p $< .001$	$b = -.03$ (-.06, .003)
IBS-SQ	$b = .17^{***}$ $p < .001$	Emotional Repres.	$b = -.32^{***}$ $p < .001$	Fr-QoL	$b = -.16^{***}$ $p < .001$	$b = .21^{***}$ p $< .001$	$b = -.05$ (-.09, -.02)
PFI Severity	$b = .55^{**}$ $p < .001$	Illness Identity	$b = -.69^{***}$ $p < .001$	Fr-QoL	$b = -.40$ $p = .30$	$b = -.78^*$ $p = .05$	$b = -.38$ (-.76, -.07)
PFI Severity	$b = .97^{**}$ $p = .004$	Emotional Repres.	$b = -.52^{***}$ $p < .001$	FR-QoL	$b = -.30$ $p = .40$	$b = -.80^*$ $p = .04$	$b = -.50$ (-.92, -.13)

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, BCB-CI* = bias-corrected bootstrap confidence intervals, $^{\diamond}$ denotes partial mediation in the c' path, $^{\diamond\diamond}$ denotes full mediation in the c' path.

3.8 Content Analysis Results: Lived Experience of PFI

The secondary aim was to explore the lived experience of PFI, specifically, to communicate the personal, social and societal consequences of PFI, and the health-related behaviours individuals implement to manage PFI. A deductive approach to the content analysis of participants free-text responses was taken, four major themes were identified, some with related subthemes, including;

- 1) **Personal Psychological Impact of PFI**, which describes the personal psychological impact of PFI, and included subthemes of; *Attitude towards PFI*; *Coping & Adjustment*; *Impact on mood*; *Understanding PFI* (see Table 17). The subtheme '*Attitude towards PFI*' includes content regarding how participants described their thoughts or beliefs towards their PFI, including factors such as motivation, determination, apathy or willpower. The subtheme '*Coping & Adjustment*' includes content where participants specifically described coping responses, their thoughts or feelings towards coping or content regarding their adjustment to PFI. The subtheme '*Impact on mood*' includes content whereby participants specifically described or mentioned a change in mood or impact on mood, including feeling low, anxious, distressed, upset, or conversely described a change in how they feel or think about themselves. The subtheme '*Understanding PFI*' includes content whereby participants described how they think about and understand their PFI.
- 2) **Social Impact of PFI**, which describes the psychological and emotional impact PFI in a social context, such as relating to how PFI impacts social gatherings or perceptions from friends and family (see Table 17). This theme includes content whereby participants mentioned perceptions from another person, or thoughts or emotions they may experience in or in relation to social situations.
- 3) **Societal Impact of PFI**, which describes the impact of having PFI in larger society and included subthemes of; *Grocery shopping* and *Convenience meals / Eating at restaurants* (see Table 17). The subtheme '*Grocery shopping*' includes content whereby participants mentioned how having PFI impacts grocery shopping or their

experiences when grocery shopping with a PFI, whereas the subtheme '*Convenience meals / Eating at restaurants*' includes content where participants described their experience or the impact of eating food 'on-the-go' or at restaurants.

- 4) **Diagnosis and Management of PFI**, which describes how individuals with PFI diagnosed and manage PFI, such as their treatment strategies and approaches and included subthemes of; *Contact with Medical Practitioners*; *Diagnosis*; *Avoidance/Restriction*; *Supplements*; *Cooking at home*; *Checking / Being careful* (see Table 17). The subtheme '*Contact with Medical Practitioners*' includes content where participants mentioned any experience when contacting or seeking help from a medical practitioner, including having input, advice, treatment plans, diagnosis or a greater understanding of PFI from a medical practitioners' involvement. The subtheme '*Diagnosis*' includes content where participants described how they came about having their PFI diagnosed, whether this was self-diagnosed or diagnosed by any other person or test. The subtheme '*Avoidance/Restriction*' includes responses and content regarding managing PFI through avoiding or restricting the offending food(s). The subtheme '*Supplements*' includes any mention of using supplements to help manage PFI and its related somatic symptoms. The subtheme '*Cooking at home*' includes content where participants identified cooking meals at home in order to manage PFI. The subtheme '*Checking / Being careful*' included responses whereby participants described using management strategies to help prevent a reaction that involved checking (checking ingredients, checking with restaurant staff, checking menus or washroom locations ahead of time), and being careful (using food diaries, timing meals).

A sample of the content analysis is included in Table 17, and all quotes are fully anonymised. The quotes from participants have been separated according to the themes and subthemes identified.

Table 17

Sample of Quotes from the Qualitative Component

<p>Personal Psychological Impact of PFI</p>	<p><u>Attitude towards PFI</u></p> <p><i>"It takes a lot of willpower and determination"</i></p> <p><i>"Sometimes I just give up and sometimes I am very determined"</i></p> <p><u>Coping & Adjustment</u></p> <p><i>"You learn to live with it, but it does affect your ability to cope especially during a flare up"</i></p> <p><i>"I accept my condition. Though I get annoyed when my symptoms flare up... shouldn't, but overall I know I can't change it and have lived with [the symptoms] for so long that it is 'normal'"</i></p> <p><i>"I have lived with [it] since my teens, I am now 63, I have learned to control it".</i></p> <p><i>"It was harder to cope with pain and some symptoms during teenage years than today"</i></p> <p><u>Impact on Mood</u></p> <p><i>"It exacerbates my anxiety"</i></p> <p><i>"I feel my emotions are quite flat on the happy/joy side since I developed the intolerance"</i></p> <p><i>"It's getting me down that I have to avoid so many foods and that I face consequences if I don't"</i></p> <p><i>"or I think I might 'get away' with [the food]. Then I regret it and feel stupid!"</i></p> <p><u>Understanding PFI</u></p> <p><i>"Understanding is limited, and I generally have to plan down time afterwards [eating an offending food]"</i></p> <p><i>"The most difficult part is not knowing precisely what food (or what amount of food) to avoid for X symptom"</i></p>
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Social Impact of PFI	<p><i>"...makes me feel like an attention seeker"</i></p> <p><i>"explaining over and over that you are trying to avoid it often draws annoying reactions from other people"</i></p> <p><i>"now people are more accepting that I have food intolerances and don't think that I am just being "weird and picky" about what I eat"</i></p> <p><i>"I feel embarrassed sometimes refusing the food people have kindly prepared"</i></p> <p><i>"It can be quite stressful and create anxiety when trying to organise things with friends or just go outside"</i></p>
Societal Impact of PFI	<p><u>Grocery Shopping</u> <i>"Shopping takes longer because I have to read labels...even of known products as some brands change the ingredients of regular products...also deciphering ...technical terms... and trying to decide if I'll take a chance or not"</i></p> <p><u>Convenience Meals / Eating at Restaurants</u> <i>"when I have to rely on convenience foods...I know I am taking a chance"</i></p> <p><i>"I get a bit anxious whenever I eat out."</i></p> <p><i>"constant need to make sure the restaurant can prepare the right food and that there are toilets available"</i></p> <p><i>"Eating out can be a problem, I become cross when it's restaurants that have limited understanding"</i></p>
Diagnosis and Management of PFI	<p><u>Contact with Medical Practitioners</u> <i>"Lack of understanding by doctors is a big limiting factor to getting effective medication"</i></p> <p><i>"I have never expected my Doctor to find a solution"</i></p> <p><i>"There isn't any input from [health professionals] to help check you're getting everything you need nutrient wise or recommend alternatives"</i></p> <p><u>Diagnosis</u> <i>"It took me a few years to realise what was wrong. I did food elimination and did get a blood test done too."</i></p> <p><i>"From my own understanding/research I feel I have this food intolerance but have not been to a clinician as it feels like it's something that they can't do anything about or test for effectively"</i></p>

Diagnosis and Management of PFI	<p><u>Avoidance/Restriction</u> <i>"I avoid foods that cause me problems but at times it doesn't make any difference as I'm still ill"</i></p> <p><i>"It requires abstaining from certain foods but it's worth the effort"</i></p> <p><i>"I tend to rely on self-directed elimination diets"</i></p> <p><u>Supplements</u> <i>"I can take lactase pills whenever I would like to eat dairy"</i></p> <p><u>Cooking at Home</u> <i>"It is much easier to eat at home or not eat when outside to avoid symptoms"</i></p> <p><u>Checking / Being Careful</u> <i>"I use "logistics" to minimise the chances of an episode, e.g. always choosing a 'safe' option from the menu, timing meals...go home straight after eating etc."</i></p> <p><i>"I kept a diary to narrow down the foods that made me break out, or gave me upset stomach, etc"</i></p>
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The results from the content analysis highlight challenges and consequences related to PFI, as detailed by individuals with PFI. Participants described the personal psychological impact of PFI, including that PFI is something that requires '*determination*' and '*willpower*' to manage, and this can be difficult to adhere to. Of interest, negative emotional effects of food avoidance were identified; individuals reported difficulty in maintaining strict avoidance, and that when offending foods are eaten, there are reports of feeling '*annoyed*', '*stupid*', and '*down*', which is in line with the quantitative findings of a tendency towards response of self-blame and disengagement. Individuals discussed the social implications of PFI, including '*drawing reactions from other people*', feelings of '*anxiety*' in the face of social plans, and '*embarrassment*' if food that others prepare is refused. Participants described how eating meals out was precarious, and associated with '*taking a chance*', feeling '*anxious*', and a '*constant need*' to check and plan ahead. The sample described a '*lack of understanding*' and lack of '*input*' from medical professionals, though there was a theme of not expecting clinicians to hold answers. Instead, individuals

described self-directed treatment by food elimination and avoidance, which nearly all respondents reported.

Of interest, an understanding of PFI may be related to how effective management is. Participants described limitations of their own understanding of PFI, which meant needing to plan for '*downtime*' and not knowing '*precisely what food or what amount to avoid to avoid symptoms*', whereas another participant described being able to take a lactase pill whenever they wanted to eat dairy products.

Across themes, behaviours including avoidance (of food, of social situations, of restaurants) and planning ahead (planning for downtime, planning restaurants that have a toilet available, timing meals, planning to go home straight after), arose as common ways individuals self-manage PFI to reduce symptoms. Of note, the only participants that shared that they had found a way to successfully manage PFI with no unintended consequences were individuals who reported lactose-intolerance managed through taking lactase enzyme supplements.

4 Discussion

This paper describes the first longitudinal study conducted to explore psychological factors reported by individuals with PFI over time, and the role of these factors in outcomes including negative affect (anxiety, distress) and poor FR-QoL. The current dissertation aimed to assess the applicability of the CSM in PFI, and quantitatively investigated the direct and mediating roles of illness perceptions, coping responses, and additional psychological and PFI-related factors associated with poor outcome in PFI. An additional aim was to qualitatively analyse the content and themes on the lived experience of PFI from free text data.

4.1 Summary of Findings

Our results lend support to our hypotheses that illness representations and coping contribute to outcome in PFI. Coping responses of self-blame and disengagement were important contributors to anxiety and distress and had mediating roles on the effect of illness perceptions. The role of illness perceptions including illness identity and emotional representations were significant contributors to poor FR-QoL, and mediators of stress, PFI severity, and symptom severity. Furthermore, findings indicate extraintestinal and GI symptom severity contributes to negative affect and poor FR-QoL, respectively. Identifying modifiable correlates of PFI is necessary in order to develop an intervention to improve outcome, and the findings have allowed for consideration of an evidence-informed intervention. The following discussion of findings will be presented with sample characteristics, followed by results separated by outcome (negative affect and FR-QoL).

4.2 Summary of Sample Characteristics

A considerable proportion of the sample were female (92.5%), which is consistent with previous research demonstrating PFI is more often reported by women (see Chapter 1). This suggests that although our sample is representative of PFI, as it is predominantly female, it is not generalisable to other populations. Characteristic findings related to PFI

are in line with findings described in Chapter 1, and additional previous research (Biesiekierski et al., 2014; Knibb et al., 2000; McGowan & Gibney, 1993; Nelson & Ogden, 2008; Nettleton et al., 2010); our sample predominantly reported symptoms in response to more than one food (71.7%), described GI and extraintestinal symptoms including bloating, stomach pain, bowel changes, fatigue and mood changes, and primarily self-diagnosed PFI (61.5%). Just under half of the sample self-reported IBS (47.8%), and those with IBS+PFI had increased functional impairment, symptom severity, and severity of PFI, reporting more offending foods, compared to individuals with PFI alone.

Self-reported depression was below clinical threshold, though above scores previously reported in PFI samples (Lillestøl, Berstad, et al., 2010; Lind, Lied, et al., 2010). Research in PFI has rarely reported case-level anxiety, however, in the current study, self-reported anxiety was above clinical threshold across all three time points. Research in PFI samples from Norway have reported average HADS-A scores at 5.3(3.7) (Lillestøl, Berstad, et al., 2010) and 4.9(3.5) (Lind, Lied, et al., 2010), compared to the current study $T1 = 9.0$ (4.9). The aforementioned research was conducted in smaller clinical samples, whereas the current study was formed of a larger non-clinical sample, who reported significantly increased anxiety. However, the average age in these two samples, 39.5 (Lillestøl, Berstad, et al., 2010) and 39.2 (Lind, Lied, et al., 2010) is similar to the average age in the current sample, which was 37.7. This suggests that results from the current community sample might be more generally representative of individuals with PFI, bearing in mind the significant proportion of women in the sample. Investigating PFI in IBS populations has established HADS-A scores above clinical threshold (Dainese et al., 2014; Nybacka et al., 2018). Less than half of the current participants reported IBS, implying that anxiety is characteristic of the sample independent of IBS. It appears self-reported anxiety is a clinically significant feature of the sample and is higher than has been previously reported in PFI populations.

Illness representations in PFI were related to one another and to subsequent coping responses. A strong illness identity, measured by the attribution of symptoms to PFI was related to emotional representations of PFI, the emotional impact of and responses to

PFI. Illness identity was additionally related to beliefs that PFI would last a long time and also that it is cyclical and unpredictable. Beliefs about consequences of PFI were strongly related to emotional representations, illness identity and timeline representations. Beliefs about control of PFI were related to improved ideas about how long PFI would last and an improved emotional response. Stronger illness coherence beliefs, relating to a better understanding of PFI, was associated with weaker emotional representations, and improved timeline cyclical beliefs, suggesting that the more someone understands PFI, the less upsetting and unpredictable they perceive it. Illness representations were understandably related to coping responses. High illness identity and emotional representations scores were related to avoidant coping responses including denial, behavioural disengagement and self-blame. Beliefs about the consequences and unpredictability of PFI were associated with behavioural disengagement, whereas stronger control and coherence beliefs were related to less disengagement.

4.3 Outcome Summary: Negative Affect

The results support our primary hypotheses, and established that illness perceptions, coping responses and additional psychological and PFI-related factors have direct associations to negative affect in PFI. The data established that this effect is stable over a 6-month period in the current sample, and the exploratory aim to use temporally ordered mediation analyses to assess suitability of the CSM was supported.

Illness perceptions including emotional representations and illness identity were most strongly associated with negative affect, including anxiety and distress, followed by beliefs about consequences, a cyclical timeline and illness coherence, at a bivariate level, which was expected and in line with research in IBS populations (Rutter & Rutter, 2002, 2007). Coping responses were more strongly correlated with anxiety and distress than illness perceptions. Coping responses of self-blame, disengagement, denial and self-distraction were associated with elevated anxiety and distress, whereas responses of positive reframing and acceptance was associated with improved affect.

Baseline multivariate linear regression models, which accounted for 42.4% - 46.3% of the variance in anxiety, and 47% - 63.2% of the variance in total distress, provided confirmation for some of the exploratory findings. However, significant findings for beliefs related consequences, illness coherence and a cyclical timeline, and a coping response of acceptance were not retained, and will be discussed. Illness perceptions of emotional representations and illness identity, and coping responses of self-blame (anxiety and distress) and disengagement (distress only) were significantly associated with negative affect, whereas positive reframing was associated with improved affect. Results additionally revealed that functional impairment (distress only) and extraintestinal symptom severity increases negative affect.

Age was included as a covariate in the anxiety models, and results from regression analyses established that a younger age was significantly associated with increased anxiety. Though this was not specifically explored in the current study, there are potential hypotheses to account for age effects supported by the findings from content analysis, which suggest a role of age and adjustment in helping to cope with PFI. Research exploring the concept of illness intrusiveness, or the illness-related disruptions in valued activities, interests and lifestyles (Dancey, Hutton-Young, Moye, & Devins, 2002; Devins et al., 1996), has demonstrated that younger-age adults appear to experience more significant distress and decreased well-being (Devins, Bezjak, Mah, Loblaw, & Gotowiec, 2006; Devins et al., 1996). It is possible that participants over 45 have lived with PFI for a longer time; analysis from the current sample indicates that participants over 45 have had PFI for an average of 22.5 years, compared to 12.4 years for participants under 45. A longer lived-experience with PFI may have equipped these participants with a better understanding of their symptoms and intolerances, or more flexible ways to cope with or adjust to lifestyle changes in PFI, though this has not been confirmed. Further, research has established that older-age adults are better able to adjust or disengage from goals and tasks that may be unattainable, and that this can be protective for well-being (Dunne, Wrosch, & Miller, 2011). In PFI this may mean that older participants are better able to adjust to or disengage from specific PFI-related contexts or self-management behaviours.

Results from the content analysis suggests that participants who had lived with symptoms since they were teenagers had '*learned to control it*' now and found '*it was harder to cope with pain and some symptoms*' when they were younger. These findings would be important to explore in future qualitative research.

Mediation analyses established that coping responses of self-blame and disengagement had a mediating role in the relationship between illness perceptions and negative affect, providing support for a study aim of testing the CSM in PFI. Path analyses revealed that coping had a stronger influence on outcome than illness perceptions, and an accumulation of evidence has established that coping responses contribute to psychological distress (Burker, Evon, Loisel, Finkel, & Mill, 2005; Carver et al., 1993; Carver & Scheier, 2002; Carver et al., 1989; Doering et al., 2004; Snow-Turek, Norris, & Tan, 1996; Wu et al., 2013), though the outcome of any coping strategy can said to be adaptive or maladaptive depending on factors such as the context in which it is used and the intent of the strategy used (Moss-Morris et al., 1996). Positive reframing was the only coping response associated with improved affect significant from regression analyses, yet showed no mediating effects, which is consistent with previous research that has found that avoidant coping responses are more strongly associated with poor outcome and distress (Brown et al., 2007; Burker et al., 2005; Carver et al., 1993; Compas et al., 2006; Doering et al., 2004; Drossman et al., 2000; Moss-Morris et al., 1996; Murberg & Bru, 2001; Scharloo et al., 1998; Snow-Turek et al., 1996; Trivedi et al., 2009).

A significant effect was found for behavioural disengagement and functional impairment specific to distress, suggesting that these were important only once the depression subscale was included in the measure of total distress. Research in clinical health populations have demonstrated an association between disengagement, depression, poor outcome, and functional impairment in clinical health populations (Brown et al., 2007; Carver et al., 1993; Compas et al., 2006; Moss-Morris et al., 1996; Murberg & Bru, 2001; Rutter & Rutter, 2002, 2007; Trivedi et al., 2009). Disengagement was associated with distress, however, as most participants had PFI for a median of 11.6 years, it is not known whether if disengagement is causal of distress, or if distress has

been experienced for a number of years and influences disengagement. In the distress mediation models, self-blame and disengagement partially mediated the effects of functional impairment, however, a subsequent model confirmed functional impairment was fully mediated by extraintestinal symptom severity. In IBS samples, depression (Ballou & Keefer, 2017; Frändemark, Törnblom, Jakobsson, & Simrén, 2018; Koloski, Boyce, Jones, & Talley, 2012) and non-GI symptoms (Frändemark et al., 2018; Koloski et al., 2012) have been associated with impaired mental and physical functioning and work-related productivity. Again, it is not possible to know the direct causality of the current findings, though future prodromal or prospective studies could address this.

Extraintestinal symptom severity appears to be an important factor in negative affect. Results from mediation analyses demonstrated significant total effects of extraintestinal symptom severity and that this was not mediated by any coping response, highlighting the significant impact of non-GI symptoms on negative affect in PFI. It is possible that extraintestinal symptoms such as fatigue, mood changes, headache, brain fog and joint pain are more distressing for individuals as they are not often an expected reaction to food and so individuals may be worried about the cause and meaning of the symptoms. Additionally, these symptoms may have a more significant impact on daily life, interfering with school, work, relationships and leisure activities. Prior research in persistent physical symptom populations have demonstrated that non-GI symptoms are often associated with psychological distress, functional limitations, less adaptive coping and poorer health outcome (Ballou & Keefer, 2017; Edwards, Dworkin, Sullivan, Turk, & Wasan, 2016; Frändemark et al., 2018; Koloski et al., 2012). The results provide support for a role of extraintestinal symptoms as associated with negative affect and functional impairment, but it is important to explore this further in future research to disentangle the mechanisms through which these relationships occur, and if there are other factors which contribute to increased extraintestinal symptom severity.

The data suggests that coping responses of self-blame and disengagement have a mediating role on the effect illness perceptions in negative affect, providing support for the CSM. The results additionally indicate that that extraintestinal symptom severity is a

significant contributor to negative affect, and not mediated by coping. A future intervention should address how self-blame and disengagement are used in PFI, and how extraintestinal symptoms are perceived and responded to, as these contribute to affect and functional impairment. It would be important to provide individuals with PFI coping skills and strategies to help self-manage symptoms and PFI-related consequences, to contribute to improved outcome.

4.4 Outcome Summary: Food Related Quality of Life

The results established that illness perceptions, coping responses and additional psychological and PFI-related factors have direct associations to FR-QoL in PFI, supporting our hypotheses. Suitability of the CSM in an outcome of FR-QoL using the SWFL as a measure was not supported.

Correlation coefficients determined illness perceptions including consequences, emotional representations and illness identity held stronger correlations to FR-QoL than coping responses. Self-blame and disengagement negatively impact FR-QoL, whereas positive reframing a situation or response was related to improved FR-QoL.

Baseline multivariate linear regression models to test the three primary hypotheses and accounted for 26.7% - 32.6% of the variance in FR-QoL. Illness identity and stronger emotional representations of PFI accounted for a higher proportion of the variance than coping responses. Positive reframing was the only coping response associated with improved FR-QoL. Results established that perceived stress, GI symptom severity and severity of PFI were additionally significantly associated with poor FR-QoL.

Mediation analyses demonstrated no significant mediating effect of positive reframing on illness representations, indicating that the hypothesised mediating role of coping in the CSM may not be suitable in FR-QoL, when using the SWFL as a measure of FR-QoL. Additional mediation models demonstrated the effects of stress were partially mediated by illness perceptions and additionally by GI symptom severity. Further, PFI severity was fully mediated by illness perceptions. Finally, the effects of increased GI symptom severity were partially mediated by emotional representations. Together, the

evidence suggests that illness identity, emotional representations, stress and GI symptoms severity are important modifiable factors to address in a future intervention to improve FR-QoL.

The experience of GI symptoms in IBS has been reported to be associated with anticipation of an unpredictable symptom episode, shame associated with losing control of bowel function, and limitations in daily life (Chang et al., 2006). In PFI, GI symptoms (which includes uncomfortable symptoms and distressing consequences) were partially mediated by emotional representations, indicating that the emotional impact of PFI influences GI symptom severity. It is possible that experience of GI symptoms negatively impacts FR-QoL as through conditioning, food and meals may become associated with a potential symptom episode and related consequences. Furthermore, a negative association between food and the experience of GI symptoms could contribute to increased stress surrounding food and meals. This is of interest, as evidence suggests that the stress response can independently modulate gut function and GI motility through gut-brain interaction, which contributes to GI symptomatology, and has been implicated in IBS and FGID (Mayer, 2000, 2011; Mayer, Craske, & Naliboff, 2001; Mayer, Naliboff, et al., 2001; Mayer & Raybould, 1990). Therefore, it is possible that seeing or thinking about offending foods or meals alone could induce a stress response and related changes in GI function, resulting in the physical and emotional experience of GI symptoms, which can impact an individual's FR-QoL. It would be important to explore these hypotheses further.

The current results provide evidence for a role of illness perceptions, stress and GI symptom severity in FR-QoL. Mediation was confirmed in other analyses, and it is possible that the CSM hypotheses were not supported in FR-QoL as a result of the measure chosen, which will be discussed. In a future psychological intervention, incorporating psychoeducation on the role of stress, stress management, and the gut-brain axis in GI symptomatology, as well strategies to manage how symptoms are perceived and responded to could potentially influence outcome.

4.5 Results Summary & Theoretical Implications

The results support our hypotheses that illness perceptions and coping both directly influence outcome, and partially support the applicability of the CSM in PFI. Overall, the findings of the study have important implications for theory, practice and future research. Over a 6-month follow-up period, there were no changes in illness perceptions, coping responses, psychological distress, FR-QoL, somatic symptom severity, perceived stress or level of functional impairment. This demonstrates the relative stability and impact of PFI over time and may imply that in our sample, the experience of PFI is not largely influenced by external stressors. Further, the results imply that how individuals think about PFI and its related symptoms and subsequently cope, may contribute to sustained poor outcome.

An aim of the study was to determine whether the CSM is an appropriate model to apply to PFI. The results established that coping responses of self-blame and disengagement had significant partial and complete mediating roles in the link between illness identity and emotional representations and negative affect. Previous research testing the CSM in allergy (Knibb & Horton, 2008) and IBS (Knowles et al., 2017; Rutter & Rutter, 2002, 2007) populations have found that coping has mediating effects between illness perceptions and psychological distress. However, coping responses did not have a significant mediating role in an outcome of FR-QoL, and illness perceptions contributed to more variance than coping. Overall, the hypothesis that coping is a mediating factor between illness representations and outcome could only partially be confirmed, and the CSM can be appropriately applied to negative affect.

Subsequent mediation models testing additional factors in PFI highlighted that coping responses had no mediating effect on extraintestinal symptom severity in anxiety or distress. An IPQ-R domain of emotional representations partially mediated the effects of GI symptom severity in FR-QoL, indicating that the emotional distress in relation to GI symptoms was an important factor in poor FR-QoL. Overall, the findings provided evidence that a hallmark feature of PFI, somatic symptoms, are a contributor of poor outcome. The experience of extraintestinal symptoms appear to be particularly important in the context of psychological distress, whereas GI symptoms impact FR-QoL. This finding

is surprising as though the experience of extraintestinal symptoms are frequently reported in PFI (see Chapter 1), research has not yet demonstrated that extraintestinal symptoms are a more significant contributor to negative affect than GI symptoms. Future research should explore this to further elucidate this relationship.

Symptom severity has been demonstrated to contribute to poor outcome and reduced QoL in IBS samples (Ballou & Keefer, 2017; Böhn et al., 2013; De Gucht, 2015; Fond et al., 2014; Frändemark et al., 2018; Jerndal et al., 2010; Knowles et al., 2017; Koloski et al., 2012; Lackner, Gudleski, Ma, et al., 2014; Lackner, Gudleski, Thakur, et al., 2014; Phillips, Wright, & Kent, 2013, 2014; Rutter & Rutter, 2002, 2007; Wolitzky-Taylor, Craske, Labus, Mayer, & Naliboff, 2012). It is worth considering why somatic symptoms specifically are an important contributor to poor outcome in PFI. Though this was not directly investigated, results from the qualitative analysis describe the direct personal consequences of PFI symptoms, including *'I don't want to go into embarrassing details of what it does to me'*, *'when I do eat something with wheat I wake up next day with a low mood'*, *'and I think to myself why do I put myself through these symptoms just for that meal of pizza or pasta?'*, and further described social consequences such as discomfort with social meals and eating at restaurants, and/or perceptions of judgement from friends and family. If symptoms are negatively appraised and associated with adverse consequences, individuals may be more likely to be vigilant towards the signs of symptoms. This is consistent with hypotheses of cognitive-emotional sensitisation (Brosschot, 2002; Eriksen & Ursin, 2002; Eriksen & Ursin, 2004; Ursin & Eriksen, 2001), somatosensory amplification (Barsky, 1979; Barsky et al., 1988; Barsky et al., 1990; Jones & Ebert, 2003; Jones et al., 2004), and visceral sensitivity (Labus et al., 2004; Labus et al., 2007). The role of visceral sensitivity in GI symptoms as contributing to poor outcome has been demonstrated in IBS (Garland et al., 2012; Knowles et al., 2017; Wolitzky-Taylor et al., 2012), and there is preliminary evidence of visceral sensitivity in PFI (Lind, Lied, et al., 2010). In addition to symptom vigilance, it is also possible that individuals may avoid contexts associated with symptoms, as is characteristic in IBS (Rønnevig, Vandvik, & Bergbom, 2009), and engage in management behaviours that would reduce symptoms,

such as food avoidance. In a 2017 study by Fitzgerald and Frankum (2017), the authors determined that intolerance was the most commonly reported reason for food avoidance and/or restriction, along with concerns that the food(s) *makes me feel sick*. Findings from the qualitative analysis of the current study revealed that individuals with PFI are likely to restrict and avoid the offending food(s) to help manage PFI. However, behaviours or goals that are difficult to adhere to, such as food avoidance, may be associated with distress if it is not successfully implemented or if there are repeated failures at an attempt to adhere to it (Dunne et al., 2011). Results from the qualitative analyses demonstrated the challenges of food avoidance, and surprisingly highlighted examples of self-blame and disengagement experienced if unable to adhere, including *'I think I might 'get away' with a bit of bread or cake. Then I regret it and feel stupid!'*; *'sometimes I just give up'*; and *'I think to myself why, do I put myself through these symptoms just for that meal'*. Though not directly measured, results of content analysis revealed that participants experience distress in relation to symptoms and symptom-related dietary and lifestyle changes, which were additionally associated with negative personal and social consequences.

The impact of consequences or control beliefs were not established at a multivariate level in the current study, which have been demonstrated to be significant in IBS (Rutter & Rutter, 2002, 2007), or illness coherence beliefs, as has been found in allergy (Knibb & Horton, 2008). Consequences of PFI were described in the qualitative component, but surprisingly, were not a significant factor from the IPQ-R. This finding is unexplained and may have had to do with the wording in the scale, however, reliability analyses demonstrated good internal consistency in the *'consequences'* subscale. It is possible that the wording on scale does not activate representations about a significant impact of PFI on daily life, or perhaps participants do not view PFI as serious or harmful condition, or with financial consequences. It is also possible that individuals do not perceive very many consequences about PFI, as symptoms are often cyclical, but the few consequences reported are more severe. However, when participants had the chance to reflect on the impact of PFI, consequences were an important part of their narrative of their experience with PFI. Strong illness coherence or control beliefs were not established,

which may reflect that currently PFI is not particularly well understood, nor does it have an established treatment. However, results from the content analysis suggest that self-directed changes in dietary habits appear to be the most common form of self-treatment that individuals maintain. Results from content analysis additionally highlighted that individuals struggle to understand the nature of their intolerance in terms of which foods specifically are symptomatic, how much of a food can they tolerate, and if there are situational or contextual factors that impact symptom experiences. The qualitative content did not align with the constructs as measured on the IPQ-R. It is possible that the wording on the scale could be adapted with better specificity for PFI in future research.

Hypothesised coping strategies of acceptance and planning, which have been associated with improved outcome in IBS and allergy (Knibb & Horton, 2008; Rutter & Rutter, 2002), were not established, though were described in the content analysis, including *“I accept my condition. Though I get annoyed when my symptoms flare up...overall I know I can't change it and have lived with [the symptoms] for so long that it is 'normal'”* and *“I use “logistics” to minimise the chances of an episode, e.g. always choosing a “safe” option from the menu, timing meals so we go home straight after eating”*. It is likely that the coping scale used did not capture or reflect how coping responses can be flexibly used or adapted depending on the specific context they are used in, and the wording of the questions did not specify a context for which coping occurs. The measurement of coping strategies has been critiqued (Skinner et al., 2003; Taylor & Stanton, 2007), and Skinner et al. (2003) identified over 400 coping behaviours measured in the literature, demonstrating challenges trying to capture the construct of coping through lower-order strategies used. It is important to identify specific coping behaviours, but perhaps to organise these according to higher-order function of the action (Skinner et al., 2003). This would be important to frame in specific PFI-related contexts, however, to better understand coping, it is likely that this information may be best attained through structured or semi-structured qualitative interviews, and this should be considered in future research.

The CSM posits a dynamic framework, whereby individuals update representations in line with new information, experiences and coping outcomes (Leventhal et al., 2016). However, the current findings established that illness representations and coping responses remained stable across all three time points, suggesting that participants did not update or change their formed illness perceptions and subsequent coping. It is possible that the number of years participants have had PFI influences these findings, and the median duration of PFI was 11.6 years. Future longitudinal research should recruit individuals with PFI at symptom onset, and measure illness perceptions, coping and related factors from this point forward, to explore whether these variables are sensitive to change around the period of adjustment.

The results additionally demonstrated that in PFI, symptoms appear to persist despite management and coping efforts. The experience of persistent symptoms is distressing and additionally contributes to poor outcome and may mean that as a result, the only information acquired, namely, the continued experience of somatic symptoms, serves to reinforce existing illness representations. The data perhaps implies some rigidity in how individuals perceive PFI and in the coping responses used, which may contribute to sustained poor outcome. It is also possible that self-management behaviours such as food avoidance, are used as it gives individuals a sense of control, however, results of the content analysis imply this also does not appear to improve outcome or reduce symptoms and may contribute to further distress, and this has also been reported in IBS (Guadagnoli et al., 2019; Jamieson, Fletcher, & Schneider, 2007). It is likely that these illness representations and coping responses used will continue to remain unchanged, unless they are targeted directly in an evidence-informed intervention.

4.6 Clinical Implications

Evidence from regression and mediation analyses suggest that specific, perhaps inflexibly held illness representations and coping responses of self-blame and disengagement could be addressed in a psychological intervention with the anticipated effect of improving outcome in PFI. The results additionally indicated that somatic

symptoms are a strong contributor of impaired functioning, psychological distress, and poor FR-QoL. PFI and IBS share sociodemographic and clinical features including anxiety and somatisation, and individuals with IBS often report PFI and vice versa (see Chapter 1). Results from the current study suggest that participants with PFI+IBS have elevated symptom severity and PFI severity and increased functional impairment, and it is possible that components of psychological interventions aimed at managing symptoms that have been successfully implemented in IBS populations may additionally be beneficial to include in any future PFI intervention. GI symptom severity in IBS is associated with poor outcome, often related to unhelpful symptom appraisals, symptom-specific and illness-related worries, avoidance behaviours including avoidance of food, and food-related, social, work, and travel situations (Rønnevig et al., 2009), and related personal and social consequences of symptoms.

A formulated cognitive-behavioural model of IBS (Spence & Moss-Morris, 2007) has allowed for the development of psychological interventions in IBS. These interventions often include psychoeducation as well as both cognitive and behavioural components to address the specific unhelpful beliefs and thoughts that are proposed to contribute to the maintenance of somatic symptoms, distress, and avoidant behaviour patterns and resultant ‘vicious circle’, and further, some have incorporated ‘third-wave’ approaches including mindfulness and acceptance (Chilcot & Moss-Morris, 2013; Ferreira, Eugenicos, Graham Morris, & Gillanders, 2011; Ferreira, Gillanders, Morris, & Eugenicos, 2018; Garland et al., 2012; Gillanders, Ferreira, Angioni, Carvalho, & Eugenicos, 2017; Ljótsson et al., 2010; Sebastián Sánchez, Gil Roales-Nieto, Ferreira, Gil Luciano, & Sebastián Domingo, 2017; Windgassen et al., 2017). It is possible that components of effective interventions in IBS may prove successful in PFI, including psychoeducation, teaching situationally functional and adaptive coping skills to help self-manage symptoms, distress and consequences of symptoms experienced in PFI, addressing specific thoughts, beliefs and avoidant behaviour patterns that may act as maintaining factors, and incorporating exposure and goal-setting for enhancing effective change (Hetterich & Stengel, 2020).

Together, this may point to the benefit of a transdiagnostic approach, within which components of an intervention could be applied as necessary, with an aim to enhance flexibility in an individuals' response to PFI and its sequelae, as well as flexibility in choosing what skill to use in various situations. In light of this, Acceptance and Commitment Therapy (ACT) might be an appropriate transdiagnostic framework (Brassington et al., 2016), which is a contextual form of CBT that aims to improve quality of life by enhancing psychological flexibility, "the ability to contact the present moment more fully as a conscious human being and, based on what the situation affords, to change or persist in behaviour in order to serve valued ends" (p.24) (Luoma, Hayes, & Walser, 2017).

The results of the current study highlighted the impact of somatic symptoms in contributing to negative affect and poor FR-QoL in PFI, and the use of self-blame and disengagement as coping strategies as contributing to anxiety and distress. ACT proposes that suffering is maintained through six core "inflexibility processes" (p.16) (Luoma et al., 2017) including experiential avoidance, which is an unwillingness to contact difficult thoughts, emotions and sensations, often leading to effort in trying to eliminate, avoid, or change these private experiences, and resulting in inflexible behaviour patterns than take people away from what matters most (Hayes & Strosahl, 2004). In the current sample, it is possible that an unwillingness to experience distressing symptoms, emotions and/or thoughts can influence the use of self-blame or disengagement and avoidance patterns, potentially maintaining poor outcome. For example, if an individual is worried about experiencing symptoms at a restaurant or social gathering, they might choose to avoid the plans all together; and as a participant described *"I feel devastated when I [become symptomatic] in public, and it does make me want to avoid going out for a long while after an episode"*. As another example, if an individual becomes symptomatic after eating, that person might blame themselves for eating that meal in the first place; this was described by a participant as *"I think I might 'get away' with a bit of bread or cake. Then I regret it and feel stupid!"*. In the first example, the decision to avoid or cancel plans is understandable given the distress experienced and feelings of shame and

embarrassment following GI distress, and avoidance effectively eliminates the chance of a distressing experience around others, however, by doing so, avoiding plans (through disengagement) may mean limitations on social and leisure activities. In the second example, self-blame provides an 'answer' for the distressing experience, though using self-blame as a problem-solving strategy can cause further unintended distress, frustration, and guilt.

Previous research in IBS using a CBT intervention identified cognitive change as a significant mediator of outcome (Chilcot & Moss-Morris, 2013), including changes in catastrophising and fear avoidance. In a traditional CBT intervention, the content of distorted thoughts would be restructured to reflect more realistic thoughts (Naliboff, Frese, & Rapgay, 2008). However, ACT proposes, through Relational Frame Theory (Barnes-Holmes & Roche, 2001) that changing how one relates to the content of their thoughts, or changing the context of how the thought is experienced, can be more effective cognitive change than attempting to change the literal content of thoughts (Hayes, 2016) (*note; a discussion of relational frame theory is outside the scope of this paper, see (Barnes-Holmes & Roche, 2001; Hayes, 2016)*). Specific cognitive practices and strategies taught in an ACT intervention can influence how sensations, thoughts, and emotions are noticed, perceived and flexibly responded to. This can change how an individual relates to their experiences and can influence functional behaviours such as contextually adaptive coping responses and re-engagement with what is valued, even in the face of difficulty, which can further drive cognitive change. An ACT intervention uses cognitive, experiential and exposure-based exercises, metaphors and between-session work focused on six flexibility processes; *present moment awareness* (non-judgmental contact with the here-and-now), *values* (clarifying chosen qualities that contribute to a personally meaningful life), *committed action* (acting in line with chosen values to support living a meaningful life), *self-as-context* (observer stance to see oneself as separate from the content of experiences and instead as the frame from which events are experienced), *defusion* (to step back from cognitions) and *acceptance* (willingness to allow all thoughts,

emotions and sensations, as an alternative to attempting to avoid, control or alter them) (Luoma et al., 2017).

ACT has been successfully evidenced in conditions with persistent physical symptoms including chronic pain (McCracken & Velleman, 2010; McCracken, Vowles, & Eccleston, 2005; Scott & McCracken, 2015; Vowles, Sowden, & Ashworth, 2014), IBS (Ferreira et al., 2011; Ferreira et al., 2018; Gillanders et al., 2017; Sebastián Sánchez et al., 2017), chronic fatigue (Ferreira et al., 2011; Jacobsen, Kallestad, Landrø, Borchgrevink, & Stiles, 2017), and in a group of adults with various long-term conditions (Brassington et al., 2016). Furthermore, ACT additionally incorporates elements of self-compassion throughout the six flexibility processes, which has been shown to contribute to improved outcome in chronic pain patients (Vowles et al., 2014).

Though the current study was not designed with an ACT framework in mind, and as a result did not include any ACT-specific outcome measures (Bond et al., 2011; McCracken, 2013; McCracken, Vowles, & Eccleston, 2004; Vowles, McCracken, McLeod, & Eccleston, 2008), a focus on acceptance of extraintestinal and GI symptoms, enhancing self-compassion, increasing flexibility in coping strategies used, and engaging in what is valued and meaningful as an alternative to avoidance fit within an ACT framework. In line with the current findings, the author proposes an ACT-based 4-session (each 90 minutes, for a total 6 hours) self-administered intervention, with therapist support. This method was selected as both a 4-session a self-administered (Lackner et al., 2008) and online-delivered (Ljótsson et al., 2010) CBT intervention has contributed to improved outcome in IBS, and there is preliminary evidence for internet-based ACT (Lappalainen et al., 2014; Simister et al., 2018), though not in an IBS population. Further, a self-administered and internet-based interventions are more convenient to both deliver and access and is an important consideration in light of the current social distancing recommendations. The proposed intervention would aim to improve the quality of life alongside difficulties, instead of trying to change difficulties, and include components evidenced in ACT-consistent interventions in IBS (Ferreira et al., 2011; Ferreira et al., 2018; Ljótsson et al., 2010) as well as psychoeducation and self-compassion to help address emotional

representations of PFI, illness identity, self-blame, disengagement, noticing and responding to symptoms, and doing what matters in the context of PFI-related distress. For a detailed intervention plan, please see Appendix XIV.

- 1) **Psychoeducation & Exploration** – including psychoeducation on the stress response, gut-brain interactions, the role of food avoidance, symptom hypervigilance, the connection between symptoms and cognitive and emotional reactions to symptoms, and exploration of the role and experience with experiential avoidance.
- 2) **Present Moment Awareness** – including mindfulness practices of (e.g. mindful eating, mindfulness around thoughts of meal and context of meals, Lovingkindness), to facilitate mindful awareness and a self-as-context (observer) position.
- 3) **Defusion** – including experiential exercises to facilitate change in how individuals relate to their thoughts instead of being fused with the content or meaning of their thoughts and stories; aiming to help individuals be able to take a step back from their thoughts and choose how they would ideally like to act in a valued direction.
- 4) **Self-as-Context** – including discussions, metaphors and exercises to help individuals see themselves as separate from the content of their experiences, from identities, labels or symptoms they assign to themselves, and from stories that define themselves based on PFI experiences.
- 5) **Acceptance** – including willingness to tolerate difficult thoughts, emotions, sensations and situations related to PFI; of symptoms if/when they show up and trying not to fight or control them; and of challenge in order to work towards change.
- 6) **Values** – including identifying and clarifying what is personally meaningful to them, and how they want to act in line with values, even in the face of difficulty.
- 7) **Committed Action** – including setting structured and meaningful goals and committing to values-based action, including exposure to challenging situations; discussing who can help on their journey and what else can help bring them towards what matters most; discussing skills such as problem-solving to overcome barriers.
- 8) **Self-Compassion** – including discussions, exercises and metaphors to facilitate a sense of self-compassion to reduce self-blame; self-compassion in the face of embarrassing

or uncomfortable symptoms; and self-compassion to continue to engage in values-based actions in light of challenges.

4.7 Strengths and Limitations

4.7.1 Strengths

The present study is strengthened by a longitudinal design. It is the first to investigate PFI and related psychological factors at multiple time points to establish unique contributors to PFI and the relative stability of the individual impact of PFI. Furthermore, the addition of the qualitative component of the study allowed for capturing a sample of the lived experience of PFI, to better understand the psychological, physical and social impact. The current sample was not clinical, thereby enhancing the generalisability of the findings to a female community population. Samples drawn from allergy, gastroenterological and medical clinics are often used in research studying individuals with PFI, which provides important information regarding other existing clinical comorbidities and allows for validating PFI, however, these samples are usually smaller in size. The study benefitted from a relatively large baseline sample ($N = 255$), and as the aims were exploratory, a large sample size adequately powered the study to be able to simultaneously examine multiple psychological and PFI-related factors that may be relevant to outcome. To date, research exploring PFI has primarily been at a bivariate and cross-sectional level, precluding drawing a causal relationship. In the current study, data was analysed at a bivariate and multivariate level; exploratory correlational analyses informed later regression models, which identified predictors to be used in confirmatory mediation models. Further, this study is strengthened by using temporally ordered data in the mediation models, which has been recommended in CSM research to better capture the dynamic processes proposed in the framework (DeLongis & Morstead, 2019).

The current study is the first to apply the CSM as a psychological framework to the experience of PFI. The results of the study provide preliminary evidence of the role of illness perceptions and coping responses as contributing to negative affect and poor FR-QoL in PFI and provides evidence for the CSM to be used as a framework for

understanding PFI and related management behaviours. Furthermore, the study identified the unique role of the experience of extraintestinal and GI symptoms and established that these are not only a significant contributor to poor outcome, but also are not readily influenced through investigated coping responses. The results were considered in the context of research in the well-studied condition IBS, in order to propose a psychological intervention with an aim to improve outcome. The findings of the current study help to advance the current understanding of PFI, and provide basis for further research, discussed under *Recommendations for Future Research*.

4.7.2 Limitations

There are several limitations;

First, though an adequate baseline sample was recruited, there was significant attrition from T1 to T3, precluding the use of T3 outcome data in temporally ordered mediation analyses. It is possible that a low incentive for participation or the sampling methodology used to recruit participants online through social media sites contributed to poor retention. Furthermore, some participants provided non-functional email addresses at baseline, and therefore it was impossible to contact them for follow-up data collection.

Second, there was missing data at each time point, resulting in data exclusion from that participant. Of interest, there were no significant differences in age or the proportion reporting IBS between those who completed all three time points, and those who did not. However, those who only completed the T1 questionnaire had significantly elevated anxiety, total distress, extraintestinal symptom severity, and GI symptom severity. The exclusion of data was not enough to significantly impact study power, data analyses or results. It is possible that this could have been rectified by the use of forced responses in the questionnaire. The decision was made to alert participants of unanswered questions, though not force a response, as some research has demonstrated that forced-response questionnaires are subject to a reactance effect and survey dropout (Stieger, Reips, & Voracek, 2007; Vicente & Reis, 2010).

Third, online questionnaires and self-report measures are subject to various response biases. Therefore, results could potentially lack validity, however, across all

outcome measures used however, results from paired t-tests and repeated measure ANOVA's demonstrated consistency in paired scores over time, suggesting relative stability of responses. Further, conducting a structured diagnostic interview would not have been feasible for the current study, or warranted given its exploratory nature, and additionally, somatic symptoms in PFI are subjectively experienced, and would be challenging for an interviewer or observer to measure.

Fourth, the measures used in the current study should be evaluated for future research, specifically A) the PSS, B) the HADS, C) a measure of FR-QoL, D) a measure of coping, and E) a measure of IBS. A) The PSS in our sample had very low internal consistency, and results from the PSS should be interpreted with caution. This finding was surprising, as the 10-item PSS, which was the measure used in the current study has demonstrated good internal consistency in previous research (Lee, 2012). B) The decision was made to use the HADS (Zigmond & Snaith, 1983), as it does not contain somatic items, the HADS-T has been demonstrated to be a good measure of distress (Norton et al., 2013) and the HADS has been used in previous research with PFI samples (see Chapter 1). Due to the large number of measures included, it was important to not increase participant burden with additional measures. However, some have argued that the HADS does not reliably differentiate between anxiety and depression (Coyne & van Sonderen, 2012; Norton et al., 2013), and that measures specifically designed to capture anxiety and depression, such as the GAD-7 (Spitzer, Kroenke, Williams, & Löwe, 2006) and PHQ-9 (Spitzer, Kroenke, Williams, & Group, 1999) respectively, are recommended. Research comparing the HADS-A and GAD-7 (Baker et al., 2018; Esser et al., 2018), and the HADS-D and PHQ-9 (Cameron, Crawford, Lawton, & Reid, 2008; Hansson, Chotai, Nordström, & Bodlund, 2009) has found that all scales have fair psychometric properties though often differed in the severity of cases captured, suggesting clinical threshold levels differ between measures. C) The SWFL was used to assess FR-QoL and provided only a general measure of how satisfied an individual is with their FR-QoL but may not have captured the specific contributors to FR-QoL in PFI. A measure for PFI specifically does not currently exist and should be considered for development in future research. D) It is likely that the

Brief-COPE did not capture the context, specificity or range of coping responses and styles in PFI and should not be considered to represent a full understanding of coping in PFI. E) The IBS measure used (Roalfe, Roberts, & Wilson, 2008) does not have established cut-off points, so it is difficult to quantify symptom severity, and scoring inconsistencies reported in literature citing this measure preclude comparison of current findings.

Sixth, the questionnaire did not include important patient-level characteristics that were found to be potentially significant in a recent systematic review (see Chapter 1), such as level of education and employment, or a measure of visceral sensitivity (Labus et al., 2004), and this was due to the current study and questionnaire being designed and built prior to attaining results of the systematic review.

Seventh, the sample was 92.5% female, limiting the generalisability of study findings to men and children. Results from previous research support the finding that PFI is predominantly reported in women, however, it is not known if this is due to underreporting in men or additional psychosocial or physiological differences that influence the subjective experience of PFI.

Finally, surprisingly, GI symptoms were not significantly associated with anxiety or distress. It is possible that GI symptom severity in PFI is not as significant of a sequela as it is reported in FGID including IBS, however, this is not possible to know from the basis of this study alone and must be explored further.

4.8 Recommendations for Future Research

Future research should explore factors that influence the onset of PFI using prospective longitudinal designs, and whether there are specific social factors that increase the risk of someone self-diagnosing a food intolerance, such as those found in the systematic review (see Chapter 1) including education level, employment history, and early living conditions. It would also be interesting to capture whether external information influences PFI, as the CSM posits that information from mass media or friends and family can influence illness perceptions (Leventhal et al., 2016). The popularisation of ‘fad diets’ that promote avoidance of particular foods and food groups, published books,

social media blogs and platforms focused on nutrition and healthy eating offer mixed and often unsubstantiated claims, and may contribute to an individual perceiving food intolerance, though this has not been specifically studied in PFI. A qualitative analysis by Hamshaw, Barnett, Gavin, and Lucas (2019) explored perceptions of expertise in social media in both FH adults and parents of children with FH, but this was regarding information seeking following diagnosis.

It is possible that the CSM has future applicability in PFI, perhaps using structured equation modelling to further explore all factors relevant in the miniaturous of PFI. Future research should consider using the Visceral Sensitivity Index (VSI) (Labus et al., 2004), which has been demonstrated to predict symptom severity in individuals with PFI (Lind, Lied, et al., 2010), and could provide the basis to target visceral sensitivity specifically in an intervention. Outcome could be measured using the GAD-7 and PHQ-9 as an alternative to the HADS, and it would be interesting to see if any differences exist in reported negative affect or in the proportion of the sample to reach clinical threshold if different measures of anxiety and depression are used.

Research should consider measuring specific PFI-related self-management behaviours, coping styles and adherence to these efforts, and additionally explore PFI-specific FR-QoL. However, to do so, it is important to develop and validate a specific PFI-related FR-QoL measure, as has been done in FA (Flokstra-de Blok et al., 2008), and IBD (Hughes et al., 2016) populations, to specifically capture what about PFI impacts FR-QoL. It would be important to recruit individuals with PFI for qualitative interviews, in order to generate items that would be specific to PFI. Interviews could consider aspects such as the impact of limited food options, having to read food labels at grocery stores, the social impact of PFI with friends and family members, the impact when dining out or when travelling, beliefs about the potential for or any existing nutrient deficiencies, and the impact of food restriction, though it would be important for participants to share aspects that may not have been considered. It would be helpful to know what individuals do as a result of their intolerance, the strategies and styles of coping, the frequency and context

of these behaviours, and how they contribute to outcome. This would be important to explore in qualitative research using structured and semi-structured interviews.

Finally, further research could include specific ACT measures of psychological flexibility and other core components of the ACT model such as experiential avoidance and acceptance, using validated measures including the Acceptance and Action Questionnaire (AAQ-II) (Bond et al., 2011) or alternatively the IBS Acceptance and Action Questionnaire (Ferreira, Eugenicos, Morris, & Gillanders, 2013), a modified Chronic Pain Acceptance Questionnaire (CPAQ) (McCracken et al., 2005; Vowles et al., 2008) and Committed Action Questionnaire (McCracken, 2013), to test the applicability of an of ACT framework in PFI, and to test the hypothesised ACT-based intervention.

4.9 Conclusions

This study was the first to longitudinally investigate psychological and PFI-related factors in individuals with self-reported food intolerance and explore how these factors uniquely impact outcomes of mood and FR-QoL. The present study provides evidence that psychological factors including illness perceptions and coping responses, and related factors of stress and symptom severity have a role in explaining poor outcome. Of the psychological variables included in the study, coping responses of self-blame and disengagement are important contributors to anxiety and distress, whereas illness perceptions including illness identity and emotional representations contribute to poor FR-QoL. The experience of extraintestinal and GI symptoms are associated with distress and poor FR-QoL, respectively, and are a defining feature of the food intolerance reaction. A psychological intervention that aims to enhance flexibility, address illness perceptions, promote contextually adaptive coping responses and incorporate acceptance of discomfort and values-based goal setting, such as one based on an ACT framework, may be of benefit to individuals with PFI who experience psychological and symptom-related distress and poor FR-QoL.

5 References

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6 Appendices

Appendix I: Letter of Ethical Approval

Research Ethics
Office

Franklin Wilkins Building
6-9 Waterloo Bridge Wing
Waterloo Road
London SE1 9NH
Telephone: 020 7848 4020/4070/4077
reo@kcl.ac.uk



Alessandra De Petrillo

27 February 2019

Dear Alessandra,

Study Title: Understanding psychological distress in individuals with perceived food intolerance: an exploratory study

Study Reference: HR-18/19-8576

I am pleased to inform you that full approval for your project has been granted by the PNM Research Ethics Subcommittee.

For your information, ethical approval has been granted for 3 years from 27 February 2019. If you need approval beyond this point, you will need to apply for an extension at least two weeks before this. You will be required to explain the reasons for the extension. However, you will not need to submit a full re-application unless the protocol has changed.

Ethical approval is required to cover the data-collection phase of the study. This will be until the date specified in this letter. However, you do not need ethical approval to cover subsequent data analysis or publication of the results. For secondary data-analysis, ethical approval is applicable to the data that is sensitive or identifies participants.

Please ensure that you follow the guidelines for good research practice as laid out in UKRIO's Code of Practice for research: <https://www.kcl.ac.uk/research/support/integrity-good-conduct/index.aspx>

Please note you are required to adhere to all research data/records management and storage procedures agreed to as part of your application. This will be expected even after the completion of the study.

If you do not start the project within three months of this letter, please contact the Research Ethics Office.

Please note that you will be required to obtain approval to modify the study. This also encompasses extensions to periods of approval. Please refer to the URL below for further guidance about the process:

<https://internal.kcl.ac.uk/innovation/research/ethics/applications/modifications.aspx>

Please would you also note that we may, for the purposes of audit, contact you from time to time to ascertain the status of your research.

If you have any query about any aspect of this ethical approval, please contact the Research Ethics Office:

<https://internal.kcl.ac.uk/innovation/research/ethics/contact.aspx>

We wish you every success with this work.

Yours sincerely,

Mr James Patterson
Senior Research Ethics Officer

For and on behalf of the PNM Research Ethics Subcommittee

Research Ethics
Office

Franklin-Wilkes Building
5.5 Waterloo Bridge Wing
Waterloo Road
London SE18 4PL
Telephone 020 7593 1000/1001/1007
reo@kcl.ac.uk



15/05/2019

Dear Alessandra,

Reference Number: RESCM-18/19-8576

Study Title: Understanding psychological distress in individuals with perceived food intolerance: an exploratory study

Modification Review Outcome: Full Approval

Thank you for submitting a modification request for the above study. This is a letter to confirm that your request has now been granted Full Approval.

If you have any questions regarding your application please contact the Research Ethics Office at reo@kcl.ac.uk.

Kind regards

Mr James Patterson

Senior Research Ethics Officer

on behalf of

PNM Research Ethics Subcommittee

Appendix II: Study Information Sheet



INFORMATION SHEET FOR PARTICIPANTS

Ethical Clearance Reference Number: HR-18/19-8576

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of study

Psychological Factors Associated with Perceived Food Intolerance: An Exploratory Study

Invitation Paragraph

I would like to invite you to participate in this research project which forms part of my research for my doctorate in Clinical Psychology (DClinPsy). Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask me if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

The purpose of this study is to explore factors, including emotions, thoughts, beliefs and symptoms, related to food intolerance, and how food intolerance influences our emotional well-being and our quality of life. This study is being conducted fully online with people who have food intolerance and can be completed from any computer or device with internet access. We wish to explore if there are any factors that might be related to food intolerance and whether these factors may also influence people's well-being. We are interested in looking at feelings like anxiety and depression, thoughts and beliefs about food intolerance, and how people cope with their condition. We would like to find out whether any of these characteristics are associated with food intolerance and if certain issues make people more or less likely to experience better or worse well-being. We hope a better psychological understanding of food intolerance will, in the long term, help health care professionals and individuals with food intolerance alike better understand and manage food intolerance.

Why have I been invited to take part?

You are being invited to participate in this study because you have identified that you might have food intolerance.

What will happen if I take part?

If you choose to take part in the study, following reading this document you may proceed to the consent form, where you will be asked to read and sign the mandatory consent questions. When this is complete, you may proceed to the survey. The survey will include questions about general information about yourself and your experience of food intolerance (e.g. age, gender, additional diagnoses, symptoms of food intolerance, aggravating foods), your mood, your beliefs about food intolerance, quality of life, coping strategies and any symptoms of Irritable Bowel Syndrome (IBS).

Participation will take place in the comfort of your own home or wherever you have access to the internet, as this is a fully online study. The survey will take **approximately 20** minutes to complete.

This study is longitudinal, which means we would like to see the changes in your experiences of food intolerance and well-being over the time. Therefore, we will ask you to complete the same questionnaires again 3 months, 6 months, and 12 months after you first completed it. It is very important to complete all questionnaires. As part of participation you will be asked to provide your email address. The provided email addresses will be only used for sending a reminder emails to remind you about the study. All data you provide will be anonymised and destroyed at the end of the study.

Do I have to take part?

Participation is completely voluntary. You should only take part if you want to and choosing not to take part will not disadvantage you in anyway. Once you have read the information sheet, please contact us if you have any questions that will help you make a decision about taking part. If you decide to participate we will ask you to sign a consent form and you will be given a copy of this consent form to keep. You may decide to withdraw from the study at any time.

Incentives

As a thank you for your participation, all participants who complete all questionnaires will be entered in a draw to win one of two £50 vouchers to www.amazon.co.uk.

What are the possible risks of taking part?

There are no potential risks of taking part in this study. If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. If you think this study has harmed you or caused you psychological stress in any way, you can contact the researchers using the contact details at the end of this information sheet in the section “**What if I have further questions, or if something goes wrong?**”. This section also includes the contact information for organisations that provide support for emotional distress.

What are the possible benefits of taking part?

There are no direct benefits gained from participating in this research. Your participation will contribute to a better understanding of food intolerance, which can help to inform psychological treatment at a later stage.

Data handling and confidentiality

Your data will be processed and stored in accordance with the General Data Protection Regulation 2016 (GDPR). Your data will be stored on a secured password-protected master database at the university. Identity in this database will be indicated by a case number, rather than by name, so you cannot be identified from it. Your data will not be shared with third parties, and you will not be identified in any publication of research results. Any information you provide will also be kept strictly confidential, as is the duty of researchers. Only the researcher (Alessandra De Petrillo) and her supervisors (Dr Emma Godfrey and Dr Lyndsay Hughes) will be able to see the provided email addresses. After data collection, information linking the case number to your email will be destroyed, which means all the provided information will be anonymous and after that point, we will be unable to identify your data. Anonymous data will be securely destroyed in five years.

Data Protection Statement

The data controller for this project will be King's College London (KCL). The University will process your personal data for the purpose of the research outlined above. The legal basis for processing your personal data for research purposes under GDPR is a 'task in the public interest' You can provide your consent for the use of your personal data in this study by completing the consent form that has been provided to you.

You have the right to access information held about you. Your right of access can be exercised in accordance with the General Data Protection Regulation. You also have other rights including rights of correction, erasure, objection, and data portability. Questions, comments and requests about your personal data can also be sent to the King's College London Data Protection Officer Mr Albert Chan info-compliance@kcl.ac.uk. If you wish to lodge a complaint with the Information Commissioner's Office, please visit www.ico.org.uk.

What if I change my mind about taking part?

You are free to withdraw at any point of the study, without having to give a reason. Withdrawing from the study will not affect you in any way. You are able to withdraw your data from the study up until April 1st, 2020, after which withdrawal of your data will no longer be possible, as all participant emails will be destroyed and information linking emails to data, thus anonymising the data. If you choose to withdraw from the study we will not retain the information you have given thus far.

What will happen to the results of the study?

The results of the study will form part of a doctoral thesis and could be published in academic journals or presented at academic conferences. A copy of the final report will be available for you at your request by emailing the research team. Also, the anonymised data set can be accessed by King's College London students for educational purposes, such as completing their final year project or master's dissertation for up to five years following study completion. However, they will not be able to access your personal information. The anonymous data set will not be shared with any third parties or made publicly available.

Who should I contact for further information?

If you have any questions or require more information about this study, please contact me using the following contact details:

Alessandra De Petrillo
alessandra.de_petrillo@kcl.ac.uk
Trainee Clinical Psychologist
Department of Psychology (PO78)
Addiction Sciences Building
Institute of Psychiatry, Psychology & Neuroscience
King's College London
SE5 8AF

What if I have further questions, or if something goes wrong?

If this study has harmed you in any way or if you wish to make a complaint about the conduct of the study you can contact King's College London using the details below for further advice and information:

Dr Emma Godfrey
emma.l.godfrey@kcl.ac.uk
Health Psychology Section, Psychology department,
IoPPN, King's College London
5th Floor Bermondsey Wing
Guy's Hospital

London Bridge
London, SE1 9RT
020 7188 0178

The following organisations provide support for individuals experiencing distress, however, should not be used in a crisis. If you have been experiencing low mood in the last two weeks, please speak to your GP.

NHS 111

Call: 111

Advice in England when you need medical help fast but it's not an emergency.

C.A.L.L Mental Health Helpline

callhelpline.org.uk

24 hour free helpline: 0800 132 737

Text: 81066

Offers emotional support and mental health information for people living in Wales.

CALM (Campaign Against Living Miserably)

0800 58 58 58 (5pm-midnight)

thecalmzone.net

Listening services, information and support for men who feel down or are in crisis.

Samaritans

Confidential, emotional support 24/7 to those experiencing despair, distress, or suicidal feelings.

Helpline: 116 123 (24 hours)

Website: www.samaritans.org.uk

Breathing Space

A free confidential helpline to call when feeling down or stressed.

Helpline: 0800 83 85 87

Website: www.breathingspace.co.uk

Thank you for reading this information sheet and for considering taking part in this research.

Appendix III: Study Consent Sheet



CONSENT FORM FOR PARTICIPANTS IN RESEARCH STUDIES

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Title of Study: *Psychological Factors Associated with Perceived Food Intolerance: An Exploratory Study*

King's College Research Ethics Committee Ref: HR-18/19-8576

Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.

I confirm that I understand that by ticking/initialling each box I am consenting to this element of the study. I understand that it will be assumed that unticked/initialled boxes mean that I DO NOT consent to that part of the study. I understand that by not giving consent for any one element I may be deemed ineligible for the study.

Please tick
or initial

☐

Please tick
or initial

1. *I confirm that I have read and understood the information sheet dated *Version 2 – 21/02/2019* for the above study. I have had the opportunity to consider the information and asked questions which have been answered to my satisfaction.

☐

2. I consent voluntarily to be a participant in this study and understand that I can refuse to answer questions and I can withdraw from the study at any time, without having to give a reason, up until April 1st 2020

☐

3. *I consent to the processing of my personal information for the purposes explained to me in the Information Sheet. I understand that such information will be handled in accordance with the terms of the General Data Protection Regulation.

☐

4. * I understand that my information may be subject to review by responsible individuals from the College for monitoring and audit purposes.

☐

5. I understand that confidentiality and anonymity will be maintained and it will not be possible to identify me in any research outputs.

☐

6. I agree that the research team may use my data for future research and understand that any such use of identifiable data would be reviewed and approved by a research ethics committee. (In such cases, as with this project, data would/would not be identifiable in any report).

☐

7. I understand that the information I have submitted will be published as a report and I wish to receive a copy of it. (In such cases, as with this project, data would/would not be identifiable in any report).

☐

8. I understand that I must not take part if I fall under the exclusion criteria as detailed in the information sheet and explained to me by the researcher.

☐

Name of Participant

Date

Signature

Name of Researcher

Date

Signature

Appendix IV: Study Questionnaire with Outcome Measures

Baseline - Psychological Factors Associated with Perceived Food Intolerance: An Exploratory Study

Basic information

Participant ID code

Please input your unique participant ID code that you created at the time of consenting to participate in the study

Reminder of code: Your unique participant ID code is a 7 (seven) character code comprised of the following

- 1) The first 3 letters of the street you live on
- 2) Two-digit birth month
- 3) The 2 letters of your Mother's first and last initials

Example: If you live on Sunset Road, were born in December and your mother's name is Jane Smith, your unique ID code would be: SUN12JS

Please select the gender that best represents you.

- ☐ Female
 - ☐ Male
 - ☐ Prefer to self-describe _____
 - ☐ Prefer not to say
-

What age are you today?

What age category best represents you?

- ☐ 18-24
 - ☐ 25-34
 - ☐ 35-44
 - ☐ 45-54
 - ☐ 55-64
 - ☐ 65-74
 - ☐ 75-84
 - ☐ 85 +
-

What ethnicity best represents you? (Office for National Statistics Categories)

- | | |
|---|--|
| <input type="radio"/> English/Welsh/Scottish/Northern Irish/British | <input type="radio"/> African |
| <input type="radio"/> Irish | <input type="radio"/> Caribbean |
| <input type="radio"/> Gypsy or Irish Traveller | <input type="radio"/> Any other Black/African/Caribbean background |
| <input type="radio"/> Any other White background | <input type="radio"/> Arab |
| <input type="radio"/> White and Black Caribbean | <input type="radio"/> Any other ethnic group |
| <input type="radio"/> White and Black African | <input type="radio"/> Pakistani |
| <input type="radio"/> White and Asian | <input type="radio"/> Bangladeshi |
| <input type="radio"/> Any other Mixed/Multiple ethnic background | <input type="radio"/> Chinese |
| <input type="radio"/> Indian | <input type="radio"/> Any other Asian background |

☐ Yes

☐ No

- ☐ Medical Professional or Allied Health Professional
- ☐ Naturopath, Nutritionist or Alternative Health Practitioner
- ☐ Results of a double-blind food challenge (if selected, specify from which practitioner under other)
- ☐ Results of a blood test (if selected, specify from which practitioner, or self-tested kit under other)
- ☐ Results of a breath test (if selected, specify from which practitioner under other)
- ☐ Results of a hair sample test or mail-in test
- ☐ Self-diagnosed
- ☐ Other _____
- ☐ Not applicable

[illegible]

If the food (s) you react to is not listed, please write the food(s) and reaction(s) below

At what age did you develop your food intolerance?

- ☐ 0-18
 - ☐ 18-24
 - ☐ 25-34
 - ☐ 35-44
 - ☐ 45-54
 - ☐ 55-64
 - ☐ 65-74
 - ☐ 75-84
 - ☐ 85+
 - ☐ Not applicable
-

We would now like to ask if you have any diagnosed **food allergies (including anaphylaxis)** that lead to **immediate** reactions? Reactions could include lip or tongue swelling, throat or chest tightening, difficulty breathing or wheezing, skin rashes or hives, rapid heart beat, dizziness or fainting or all of the above after consuming the allergenic food(s), and can occur within minutes - two hours after exposure to the food(s).

- ☐ Yes
 - ☐ No
-

Do you have an EpiPen?

- ☐ Yes
 - ☐ No
-

How were you diagnosed with your food allergy?

- ☐ Medical Professional or Allied Health Professional
 - ☐ Naturopath, Nutritionist or Alternative Health Practitioner
 - ☐ Results of a double-blind food challenge
 - ☐ Results of a blood test
 - ☐ Results of a breath test
 - ☐ Results of a hair sample test or mail-in test
 - ☐ Self-diagnosed
 - ☐ Other _____
 - ☐ Not applicable
-

Please select any/all of the reactions that you experience following exposure to foods you are allergic to.

	Egg	Shellfish and/or Seafood	Wheat	Gluten	Milk	Peanut	Treenut (incl. walnut, almond, hazelnut, cashew, pistachio and Brazil nuts)	Soya	Sesame and other seeds	Other
Skin / Oral reactions (hives, lip or tongue swelling, difficulty swallowing, throat tightening)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Respiratory reactions (chest tightening, trouble breathing, wheezing)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Gastrointestinal reactions (vomiting)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cardiovascular reactions (chest pain, rapid heartbeat, fainting, low blood pressure)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

If the food (s) you react to is not listed, please write the food(s) and reaction(s) below

At what age did you develop your food allergy?

- ☐ 0-18
- ☐ 18-24
- ☐ 25-34
- ☐ 35-44
- ☐ 45-54
- ☐ 55-64
- ☐ 65-74
- ☐ 75-84
- ☐ 85+
- ☐ Not applicable

Do you have Coeliac disease? Coeliac disease is an autoimmune condition that causes inflammation and damage to the small intestine after ingesting gluten. Coeliac disease is not gluten sensitivity.

- ☐ Yes
- ☐ No
- ☐ Don't know

If yes, how were you diagnosed with Coeliac disease?

- ☐ Positive biopsy
- ☐ Results of a blood test
- ☐ Other _____

Do you have Irritable Bowel Syndrome (IBS)? IBS is condition of the digestive system consisting of frequent abdominal discomfort and bowel symptoms.

- ☐ Yes
- ☐ No
- ☐ Don't know

If yes, how were you diagnosed with IBS?

- ☐ Medical practitioner
- ☐ Self-Diagnosed
- ☐ Other _____
- ☐ Not applicable

Have you ever been diagnosed by a medical professional / allied health professional for any of the following conditions? Please select all that apply.

- ☐ Asthma
- ☐ Ectopic/atopic dermatitis
- ☐ Hay fever/ allergic rhinitis / seasonal allergies
- ☐ Insect sting allergy
- ☐ Latex allergy
- ☐ Medication allergy
- ☐ Urticaria/Hives
- ☐ Not applicable

Is there anything else that you would like to tell us about your food intolerance or food allergy? Max. 300 characters.

End of Block: Basic information

IPQ-R

Listed below are a number of **symptoms** that you may or may not have experienced since your food intolerance. Please indicate by clicking Yes or No , whether you have experienced any of these symptoms since your food intolerance, and whether you believe that these symptoms are related to your food intolerance.

	I have experienced this symptom since my food intolerance.		This symptom is related to my food intolerance.	
	Yes	No	Yes	No
Pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Sore Throat	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Nausea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Breathlessness	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Weight Loss	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Fatigue	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Stiff Joints / Joint Pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Sore Eyes	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Wheeziness	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Headaches	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Upset Stomach	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Dizziness	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Loss of Strength	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Brain Fog	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

We are interested in your own **personal views** of how you now see your food intolerance.
Please indicate how much you agree or disagree with the following statements about food intolerance by
ticking the appropriate box

	Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
1. My food intolerance will last a short time.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. My food intolerance is likely to be permanent rather than temporary.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. My food intolerance will last for a long time.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. My food intolerance will pass quickly.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. I expect to have this for the rest of my life.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. My food intolerance is a serious condition.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. My food intolerance has major consequences on my life.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. My food intolerance does not have much effect on my life.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. My food intolerance strongly affects the way others see me.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. My food intolerance has serious financial consequences.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
11. My food intolerance causes difficulties for those who are close to me.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
12. There is a lot which I can do to control my symptoms.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
13. What I can do can determine whether my food intolerance gets better or worse.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
14. The course of my food intolerance depends on me.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
15. Nothing I do will affect my food intolerance.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
16. I have the power to influence my food intolerance.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
17. My actions will have no effect on the outcome of my food intolerance.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

18. My food intolerance will improve in time.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
19. There is very little that can be done to improve my food intolerance.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
20. My treatment will be effective in curing my food intolerance.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
21. The negative effects of my food intolerance can be prevented (avoided) by my treatment	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
22. My treatment can control my food intolerance.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
23. There is nothing which can help my food intolerance.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
24. The symptoms of my food intolerance are puzzling to me.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
25. My food intolerance is a mystery to me.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
26. I don't understand my food intolerance.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
27. My food intolerance doesn't make any sense to me.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
28. I have a clear picture or understanding of my food intolerance.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
29. The symptoms of my food intolerance change a great deal from day to day.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
30. My symptoms come and go in cycles.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
31. My food intolerance is very unpredictable.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
32. I go through cycles in which my food intolerance gets better and worse.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
33. I get depressed when I think about my food intolerance.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
34. When I think about my food intolerance I get upset.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

35. My food intolerance makes me feel angry.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
36. My food intolerance does not worry me.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
37. Having this food intolerance makes me feel anxious.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
38. My food intolerance makes me feel afraid.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

We are interested in what you consider may have been the **cause of your food intolerance**. As people are very different, there is no correct answer for this question. We are most interested in your own views about the factors that caused your illness rather than what others including doctors or family may have suggested to you. Below is a list of possible causes for your **food intolerance**. Please think of each question in relation to your **food intolerance**.

Please indicate how much you agree or disagree that they were causes for you by ticking the appropriate box

	Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
1. Stress or worry	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. Hereditary - it runs in my family	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. A germ or virus	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. Diet or eating habits	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. Chance or bad luck	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. Poor medical care in my past	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. Pollution in the environment	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. My own behaviour	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. My mental attitude (e.g. thinking about life negatively)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. Family problems or worries caused my food intolerance	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
11. Overwork	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
12. My emotional state (e.g. feeling down, lonely, anxious, empty)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
13. Ageing	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
14. Alcohol	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
15. Smoking	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
16. Accident or injury	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
17. My personality	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
18. Altered immunity	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

In the table below, please list in rank-order the three most important factors that you now believe caused YOUR food intolerance. You may use any of the items from the list above, or you may have additional ideas of your own.

The most important causes for me:

- ☐ 1 _____
- ☐ 2 _____
- ☐ 3 _____

End of Block: IPQR

SWFL

Please think of all the things you do and experience in relation to food and meals (e.g., planning meals, shopping, preparing meals, eating meals) and then, using the scale below, indicate your agreement with each item. **Please think of each question in relation to your food intolerance.**

	Strongly Disagree (1)	Disagree (2)	Slightly Disagree (3)	Neither agree nor disagree (4)	Slightly Agree (5)	Agree (6)	Strongly Agree (7)
1. Food and meals are positive elements in my life	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. When I think of my next meal, I only see problems, obstacles and disappointments	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. I am generally pleased with my food	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. Food and meals give me satisfaction in daily life	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. My life in relation to food and meals is close to my ideal	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. I wish my meals were a much more pleasant part of my life	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. With regard to food, the conditions of my life are excellent	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

End of Block: SWFL

HADS

Please think of what you have experienced in the past week for these next questions.

Tick the box beside the reply that is closest to how you have been feeling **in the past week**. Don't take too long over your replies: your immediate response is best.

I feel tense or 'wound up'

- ☐ Most of the time
- ☐ A lot of the time
- ☐ From time to time, occasionally
- ☐ Not at all

I still enjoy the things I used to enjoy

- ☐ Definitely as much
- ☐ Not quite so much
- ☐ Only a little
- ☐ Hardly at all

I get a sort of frightened feeling as if something awful is about to happen

- ☐ Yes definitely and quite badly
- ☐ Yes but not too badly
- ☐ A little, but it doesn't worry me
- ☐ Not at all

I can laugh and see the funny side of things

- ☐ As much as I always could
- ☐ Not quite so much now
- ☐ Definitely not so much now
- ☐ Not at all

Worrying thoughts go through my mind

- ☐ A great deal of the time
- ☐ A lot of the time
- ☐ From time to time, but not too often
- ☐ Only occasionally

I feel cheerful

- ☐ Not at all
- ☐ Not often
- ☐ Sometimes
- ☐ Most of the time

I can sit at ease and feel relaxed

- ☐ Definitely
- ☐ Usually
- ☐ Not often
- ☐ Not at all

I feel as if I am slowed down

- ☐ Nearly all the time
- ☐ Very often
- ☐ Sometimes
- ☐ Not at all

I get a sort of frightened feeling like 'butterflies' in the stomach

- ☐ Not at all
- ☐ Occasionally
- ☐ Quite often
- ☐ Very often

I have lost interest in my appearance

- ☐ Definitely
- ☐ I don't take as much care as I should
- ☐ I may not take quite as much care
- ☐ I take just as much care as ever

I feel restless as if I have to be on the move

- ☐ Very much indeed
- ☐ Quite a lot
- ☐ Not very much
- ☐ Not at all

I look forward with enjoyment to things

- ☐ As much as I ever did
- ☐ Rather less than I used to
- ☐ Definitely less than I used to
- ☐ Hardly at all

I get sudden feelings of panic

- ☐ Very often indeed
- ☐ Quite often
- ☐ Not very often
- ☐ Not at all

I can enjoy a good book or radio or TV program

- ☐ Often
- ☐ Sometimes
- ☐ Not often
- ☐ Very seldom

End of Block: HADS

WSAS

People's health difficulties sometimes affect their ability to do certain day-to-day tasks in their lives. Look at each section and determine on the scale provided how much your food intolerance impairs your ability to **carry out daily activities**. Please think of each question in relation to your food intolerance.

	Not at all (0)	(1)	Slightly (2)	(3)	Definitely (4)	(5)	Markedly (6)	(7)	Very severely (8)
1. My ability to work is impaired. '0' means 'not at all impaired' and '8' means very severely impaired to the point I can't work	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. My home management (cleaning, tidying, shopping, cooking, looking after home or children, paying bills) is impaired	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. My social leisure activities (with other people e.g. parties, bars, clubs, outings, visits, dating, home entertaining) are impaired	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. My private leisure activities (done alone, such as reading, gardening, collecting, sewing, walking alone) are impaired	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. My ability to form and maintain close relationships with others, including those I live with, is impaired	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

End of Block: WSAS

PHQ-15

Please think of symptoms you have experienced during the past 4 weeks for these next questions. Please think of each question in relation to your food intolerance.

During the **past 4 weeks**, how much have you been bothered by any of the following problems?

	Not bothered at all	Bothered a little	Bothered a lot
1. Stomach pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. Back pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. Pain in your arms, legs, or joints (knees, hips, etc.)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. Menstrual cramps or other problems with your periods (men leave blank)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. Headaches	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. Chest pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. Dizziness	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. Fainting spells	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. Feeling your heart pound or race	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. Shortness of breath	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
11. Pain or problems during intercourse	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
12. Constipation, loose bowels, or diarrhea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
13. Nausea, gas, or indigestion	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
14. Feeling tired or having low energy	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
15. Trouble sleeping	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

End of Block: PHQ-15

Birmingham IBS Symptom Questionnaire

These questions ask you about any abdominal and bowel symptoms. When we use the word abdomen we mean belly/tummy. Some of the questions ask about passing a stool. By this we mean going to the toilet for a reason other than to urinate (pass water). All of these questions refer to what you have experienced **during the last 4 weeks**. Please select one box for each statement.

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
1. During the last 4 weeks, how often have you had discomfort or pain in your abdomen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. How often have you been troubled with loose, mushy or watery bowel motions during the last 4 weeks?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. How often during the last 4 weeks have you been troubled with diarrhoea?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. During the last 4 weeks how often have you been troubled by hard bowel motions?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. During the last 4 weeks how often have you felt the need to strain to pass a motion (stool)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. During the last 4 weeks how often have you been troubled by constipation?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. During the last 4 weeks how often did you experience pain or discomfort in your abdomen after eating?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. How often has your abdominal pain prevented you from sleeping, or woken you during the night during the last 4 weeks?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. During the last 4 weeks how often have you leaked or soiled yourself?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. How often during the last 4 weeks have you suffered from a feeling of urgency (feeling that you must immediately rush to the toilet to pass a stool)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
11. How often have you passed mucus or slime in your stools over the last 4 weeks?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

End of Block: Birmingham IBS

Brief COPE

These items deal with ways you've been coping with the stress in your life. There are many ways that people try to cope with their difficulties. Don't answer on a basis of whether it seems to be working or not - just whether or not you're doing it.

	I haven't been doing this at all	I've been doing this a little bit	I've been doing this a medium amount	I've been doing this a lot
1. I've been turning to work or other activities to take my mind off things.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. I've been concentrating my efforts on doing something about it.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. I've been saying to myself "this isn't real."	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. I've been using alcohol or other drugs to make myself feel better.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. I've been getting emotional support from others.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. I've been giving up trying to deal with it.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. I've been taking actions to try and make the situation better.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. I've been refusing to believe that it is happening.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. I've been saying things to let my unpleasant feelings escape.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. I've been getting help and advice from other people.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
11. I've been using alcohol or other drugs to help me get through it.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
12. I've been trying to see it in a different light, to make it seem more positive.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
13. I've been criticizing myself.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
14. I've been trying to come up with a strategy about what to do.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
15. I've been getting comfort and understanding from someone.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
16. I've been giving up the attempt to cope.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
17. I've been looking for something good in what is happening.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
18. I've been making jokes about it.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

19. I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, or shopping.

☐

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☐

20. I've been accepting the reality of the fact that it is happening.

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21. I've been expressing my negative feelings.

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22. I've been trying to find comfort in my religion or spiritual beliefs.

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23. I've been trying to get advice or help from other people.

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24. I've been learning to live with it.

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25. I've been thinking about what steps to take.

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26. I've been blaming myself for things that happened.

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27. I've been praying or meditating.

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28. I've been making fun of the situation.

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☐

PSS

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate by selecting how often you felt or thought a certain way.

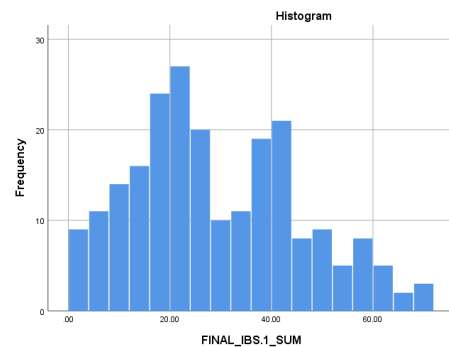
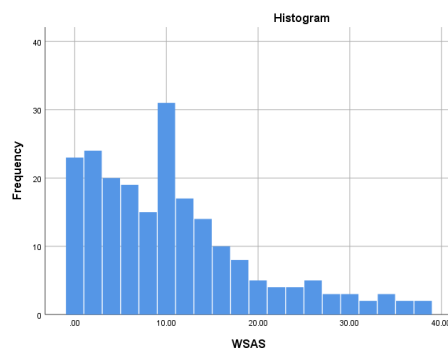
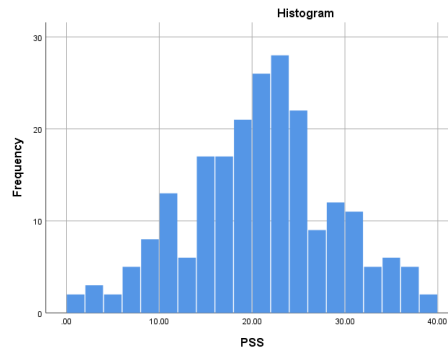
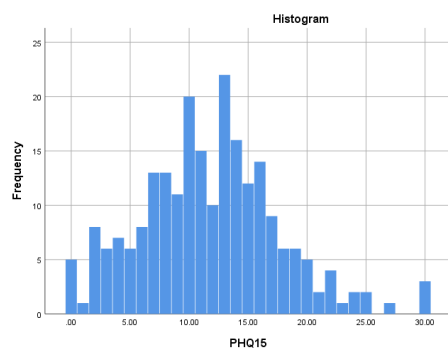
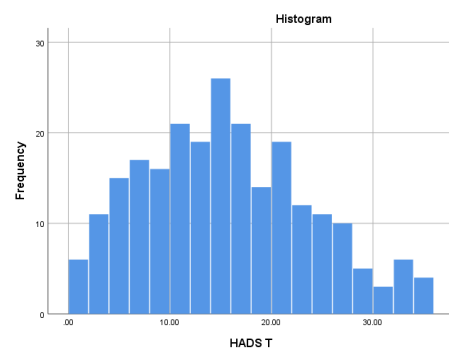
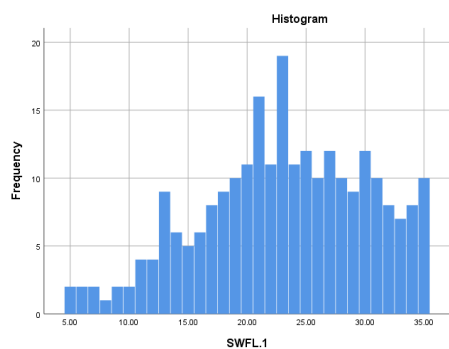
	Never	Almost Never	Sometimes	Fairly Often	Very Often
1. In the last month, how often have you been upset because of something that happened unexpectedly?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. In the last month, how often have you felt that you were unable to control the important things in your life?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. In the last month, how often have you felt nervous and stressed?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. In the last month, how often have you felt confident about your ability to handle your personal problems?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. In the last month, how often have you felt that things were going your way?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. In the last month, how often have you found that you could not cope with all the things that you had to do?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. In the last month, how often have you been able to control irritations in your life?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. In the last month, how often have you felt that you were on top of things?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. In the last month, how often have you been angered because of things that happened that were outside of your control?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

End of Block: PSS

You are just about finished this survey! Before you go, is there anything else that you would like to tell us about your food intolerance or your experience with food intolerance?

Thank you very much for your participation!

Appendix V: Histograms



Appendix VI: Group Analysis Separated by Identify Female vs. Not Identify Female

	Total N = 255	Identify Female N = 236	Identify not- female N = 19	Statistical Test & P Value
<i>Sociodemographic Characteristics</i>		n (%)	n (%)	
18-44	163 (63.9%)	147 (57.6%)	16 (6.3%)	$\chi^2 = 3.67, p = .04, \phi = .12$
45-84	92 (36.1%)	89 (34.9%)	3 (1.2%)	
PFI Only	194 (76.1%)	182 (71.4%)	12 (4.7%)	$\chi^2 = 1.75, p = .15, \phi = .08$
PFI & FA	61 (23.9%)	54 (21.2%)	7 (2.7%)	
White	230 (90.2%)	216 (84.7%)	14 (5.5%)	$\chi^2 = 6.33, p = .012, \phi = .16$
Black/Minority Ethnic	25 (9.8%)	20 (8.5%)	5 (26.3%)	
<i>Clinical Characteristics</i>		n (%)	n (%)	
Irritable Bowel Syndrome	122 (47.8%)	112 (55.2%)	10 (4.9%)	$\chi^2 = .042, p = .84, \phi = -.01$
Coeliac Disease	19 (8.6%)	17 (7.7%)	2 (0.9%)	$\chi^2 = .33, p = .57, \phi = -.04$
<i>Baseline Scores</i>	M (SD)	M (SD)	M (SD)	
SWFL	23.1 (7.0)	23.3 (6.9)	21.8 (9.3)	$t(17.35) = .65, p = .52$
HADS Anxiety	9.0 (4.9)	8.9 (4.9)	10.5 (5.2)	$t(237) = 1.28, p = .24$
HADS Depression	5.9 (4.4)	5.8 (4.3)	8.2 (5.5)	$t(236) = 2.19, p = .030$
HADS Total	15.0 (8.0)	14.7 (8.3)	18.7 (10.0)	$t(235) = 1.88, p = .062$
WSAS	10.2 (9.1)	10.1 (10.5)	11.7 (11.2)	$t(232) = .61, p = .54$
PHQ-15	11.7 (5.9)	11.8 (5.9)	11.8 (6.0)	$t(230) = .08, p = .93$
Birmingham IBS Scale	28.7 (17.4)	28.8 (17.4)	28.1 (17.1)	$t(223) = -.149, p = .88$
PSS	20.4 (7.9)	20.4 (7.8)	20.4 (9.1)	$t(222) = .04, p = .97$
<i>Baseline Caseness</i>	n (%)	n (%)	n (%)	
HADS Anxiety	140 (59.6%)	128 (58.7%)	12 (70.6%)	$\chi^2 = .92, p = .34, \phi = -.06$
HADS Depression	76 (32.5%)	68 (31.3%)	8 (47.1%)	$\chi^2 = 1.78, p = .18, \phi = -.09$
WSAS	95 (41.3%)	88 (41.3%)	7 (41.2%)	$\chi^2 = .00, p = .99, \phi = .001$

Appendix VII: Group Analysis Separated by PFI-Only vs PFI + FA

	Total N = 255	PFI Only N = 194	PFI and FA N = 61	Statistical Test & P Value
<i>Sociodemographic Characteristics</i>		n (%)	n (%)	
18-44	163 (63.9%)	119 (46.7%)	44 (17.3%)	$\chi^2 = 2.60, p = .11, \phi = -.10$
45-84	92 (36.1%)	75 (29.4%)	17 (6.7%)	
Identify Female	236 (92.5%)	182 (71.4%)	54 (21.2%)	$\chi^2 = 1.88, p = .17, \phi = -.09$
White	230 (90.2%)	178 (69.8%)	52 (20.4%)	$\chi^2 = 2.22, p = .14, \phi = -.09$
Black/Minority Ethnic	25 (9.8%)	16 (6.3%)	9 (3.5%)	
<i>Clinical Characteristics</i>		n (%)	n (%)	
Irritable Bowel Syndrome	122 (47.8%)	103 (50.7%)	19 (9.4%)	$\chi^2 = 7.71, p = .006, \phi = -.20$
Coeliac Disease	19 (8.6%)	11 (5%)	8 (2.6%)	$\chi^2 = 3.69, p = .055, \phi = .13$
<i>Baseline Scores</i>	M (SD)	M (SD)	M (SD)	
SWFL	23.1 (7.0)	23.5 (6.6)	21.9 (8.5)	$t(81.98) = 1.29, p = .20$
HADS Anxiety	9.0 (4.9)	8.8 (4.8)	9.8 (5.1)	$t(231) = -1.44, p = .15$
HADS Depression	5.9 (4.4)	5.9 (4.5)	6.2 (4.2)	$t(230) = -.54, p = .59$
HADS Total	15.0 (8.0)	14.7 (8.3)	16.0 (8.6)	$t(229) = -1.04, p = .30$
WSAS	10.2 (9.1)	10.1 (10.0)	10.9 (12.3)	$t(78.06) = -.49, p = .62$
PHQ-15	11.7 (5.9)	11.5 (5.8)	12.6 (6.4)	$t(224) = -1.18, p = .24$
Birmingham IBS Scale	28.7 (17.4)	29.6 (16.6)	29.1 (19.5)	$t(220) = .111, p = .86$
PSS	20.4 (7.9)	19.9 (7.8)	22.1 (8.0)	$t(218) = -1.82, p = .07$
<i>Baseline Caseness</i>	n (%)	n (%)	n (%)	
HADS Anxiety	140 (59.6%)	103 (57.9%)	37 (64.9%)	$\chi^2 = .89, p = .36, \phi = .06$
HADS Depression	76 (32.5%)	54 (30.5%)	22 (38.6%)	$\chi^2 = 1.29, p = .26, \phi = .07$
WSAS	95 (41.3%)	74 (42.3%)	21 (38.2%)	$\chi^2 = .29, p = .59, \phi = -.04$

Appendix VIII: Group Analysis Separated by PFI-Only vs IBS + PFI

	Total N = 255	PFI Only N = 133	IBS + PFI N = 122	Statistical Test & P Value
<i>Sociodemographic Characteristics</i>		n (%)	n (%)	
Identifies Female	236 (92.5%)	124 (93.2%)	112 (91.8%)	$\chi^2 = .1, p = .66, \phi = -.03$
18-44	163 (63.9%)	87 (65.4%)	76 (62.3%)	$\chi^2 = .268, p = .60, \phi = .03$
45-84	92 (36.1%)	46 (34.6%)	46 (37.7%)	
PFI Only	194 (76.1%)	91 (68.4%)	103 (84.4%)	$\chi^2 = 8.96, p = .003, \phi = -.19$
PFI & FA	61 (23.9%)	42 (31.6%)	19 (15.6%)	
White	230 (90.2%)	119 (89.5%)	111 (91%)	$\chi^2 = 164, p = .69, \phi = .03$
Black/Minority Ethnic	25 (9.8%)	14 (10.5%)	11 (29%)	
<i>Clinical Characteristics</i>		n (%)	n (%)	
Coeliac Disease	19 (8.6%)	10 (8.5%)	9 (8.7%)	$\chi^2 = .003, p = .96, \phi = .003$
# of Offending Foods				
1 food	72 (28.3%)	52 (39.1%)	23 (18.9%)	
2 foods	59 (23.5%)	33 (24.8%)	26 (21.3%)	
3 foods	55 (21.7%)	21 (15.8%)	34 (27.8%)	
4+ foods	67 (26.5%)	27 (20.3%)	39 (32%)	
<i>Baseline Scores</i>	M (SD)	M (SD)	M (SD)	
SWFL	23.1 (7.0)	23.7 (7.7)	22.3 (6.3)	$t(239) = 1.75, p = .08$
HADS Anxiety	9.0 (4.9)	8.8 (5.0)	9.2 (4.7)	$t(233) = -.73, p = .47$
HADS Depression	5.9 (4.4)	5.9 (4.5)	6.1 (4.3)	$t(232) = -.31, p = .76$
HADS Total	15.0 (8.0)	14.8 (8.3)	15.3 (7.6)	$t(231) = -.67, p = .50$
WSAS	10.2 (9.1)	9.4 (9.4)	11.8 (8.7)	$t(228) = -2.3, p = .02$
PHQ-15	11.7 (5.9)	10.6 (5.8)	12.9 (5.8)	$t(226) = -.30, p = .003$
Birmingham IBS Scale	28.7 (17.4)	23.5 (15.4)	34.3 (16.7)	$t(220) = -5.43, p = .00$
PSS	20.4 (7.9)	19.99 (7.9)	20.8 (7.7)	$t(218) = -.77, p = .45$
<i>Baseline Caseness</i>	n (%)	n (%)	n (%)	
HADS Anxiety	140 (59.6%)	68 (57.1%)	72 (62.1%)	$\chi^2 = .59, p = .44, \phi = .05$
HADS Depression	76 (32.5%)	40 (33.6%)	36 (31.3%)	$\chi^2 = .14, p = .71, \phi = -.03$
WSAS	95 (41.3%)	38 (32.8%)	56 (49.1%)	$\chi^2 = .64, p = .01, \phi = .17$

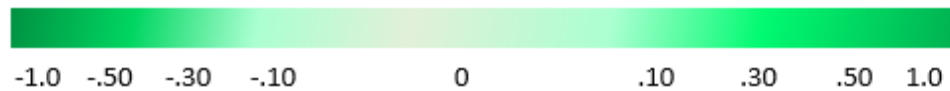
Appendix IX: Additional Causal Attributions of PFI

Gut health	<i>'gut health'; 'microbiome'; 'imbalanced gut physiology'; 'damaged gut health'; 'gut damage from modern diet'; 'intestinal changes'; 'stomach bacteria'; 'gut bacteria imbalance'; 'stomach lining'; 'microbiome deficiency'</i>
Previous Health Conditions	<i>'past anorexia'; 'anorexia nervosa'; 'past cancer and treatment'; 'polycystic ovarian syndrome'; 'Hashimoto'; 'fibromyalgia'; 'autoimmune condition'; 'binge eating in youth'; 'thyroid problems'; 'acquired brain injury'; 'chemotherapy'; 'diabetes'</i>
Medication	<i>'contraceptive pill'; 'hormonal therapy'; 'medication'; 'antibiotics'; 'overuse of antibiotics'; 'anti-inflammatories'</i>

Appendix X: IPQ-R, Brief-COPE and Outcome Correlational Analysis

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
1) HADS-A	1																								
2) HADS-T	.913**	1																							
3) SWFL	-.325**	-.388**	1																						
4) Self-Distract	.282**	.287**		1																					
5) Active Coping	-0.050	-0.063	0.090	.294**	1																				
6) Denial	.333**	.364**	-0.074	.307**	0.085	1																			
7) Substance Use	.188**	.216**	-0.025	.352**	0.012	.190**	1																		
8) Emotional Support	0.113	0.068	0.021	.396**	.367**	.145*	0.036	1																	
9) Instrumental Support	0.098	0.082	0.031	.422**	.425**	.174**	0.076	.793**	1																
10) Disengagement	.455**	.555**	-.276**	.237**	-.159*	.417**	.232**	0.041	0.006	1															
11) Venting	.182**	.198**	-0.023	.379**	.230**	.405**	.183**	.453**	.439**	.278**	1														
12) Positive Reframe	-.184**	-.219**	.214**	.231**	.489**	.165*	-0.016	.331**	.419**	-.153*	.256**	1													
13) Planning	-0.021	-0.030	0.101	.371**	.694**	0.129	0.109	.410**	.471**	-0.094	.262**	.451**	1												
14) Humour	0.075	0.028	0.049	.339**	.219**	.161*	.139*	.231**	.255**	0.092	.361**	.349**	.177**	1											
15) Acceptance	-0.113	-.157*	0.094	.182**	.397**	-0.067	-0.027	.186**	0.113	-0.075	0.085	.384**	.437**	.246**	1										
16) Religion	0.009	0.020	0.029	.170**	0.098	.240**	-0.029	.273**	.316**	0.031	.173**	.241**	.139*	0.066	-0.008	1									
17) Self-Blame	.534**	.559**	-.265**	.430**	0.019	.383**	.249**	.192**	.185**	.599**	.422**	-0.061	0.115	.134*	-0.035	0.089	1								
18) Identity	.243**	.268**	-.363**	.161*	0.059	.253**	0.123	0.047	0.067	.251**	0.130	0.030	.157*	.149*	0.116	0.061	.187**	1							
19) Timeline Acute/Chronic	-0.008	0.019	-.169**	0.061	-0.030	-0.035	-0.023	-0.008	-0.014	0.084	0.007	-0.091	-0.003	-0.019	0.051	-.158*	0.085	.197**	1						
20) Timeline Cyclical	.229**	.207**	-.207**	-0.055	-0.057	0.042	-0.007	0.070	0.025	.176**	0.034	-0.096	-0.024	-0.050	-0.125	0.040	0.088	.237**	-.183**	1					
21) Consequences	.174**	.236**	-.432**	0.015	0.082	0.074	0.011	0.022	0.004	.213**	0.067	-0.067	0.014	-0.005	0.081	0.000	.140*	.475**	.402**	.159**	1				
22) Personal Control	-0.057	-0.070	.142*	-0.040	0.124	-0.044	0.003	-0.101	-0.045	-.186**	-0.002	0.100	0.055	0.012	0.096	0.049	-.140*	-0.089	-.251**	0.083	-.162**	1			
23) Treatment Control	-0.081	-0.103	.148*	-0.021	.163*	-0.122	0.114	-0.031	0.032	-.203**	-0.023	.136*	.152*	0.082	0.079	0.044	-.132*	-.126*	-.377**	0.089	-.213**	.570**	1		
24) Illness Coherence	-.176**	-.187**	.142*	0.024	-0.014	-0.092	0.049	0.006	-0.011	-.173**	-0.022	0.095	0.004	0.039	0.128	-0.125	-.148*	-0.105	.184**	-.450**	-.124*	0.112	0.043	1	
25) Emotional Representations	.364**	.401**	-.412**	0.083	0.089	.169**	0.024	0.076	0.042	.287**	.167*	-.138*	0.042	-0.086	-0.060	0.033	.224**	.322**	.244**	.309**	.701**	-.208**	-.223**	-.287**	1

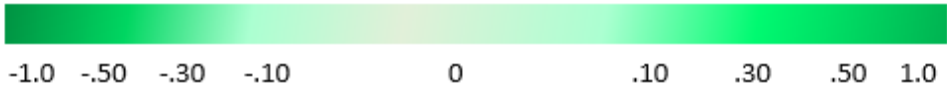
*only correlations significant at 0.01 level (2-tailed) are shaded



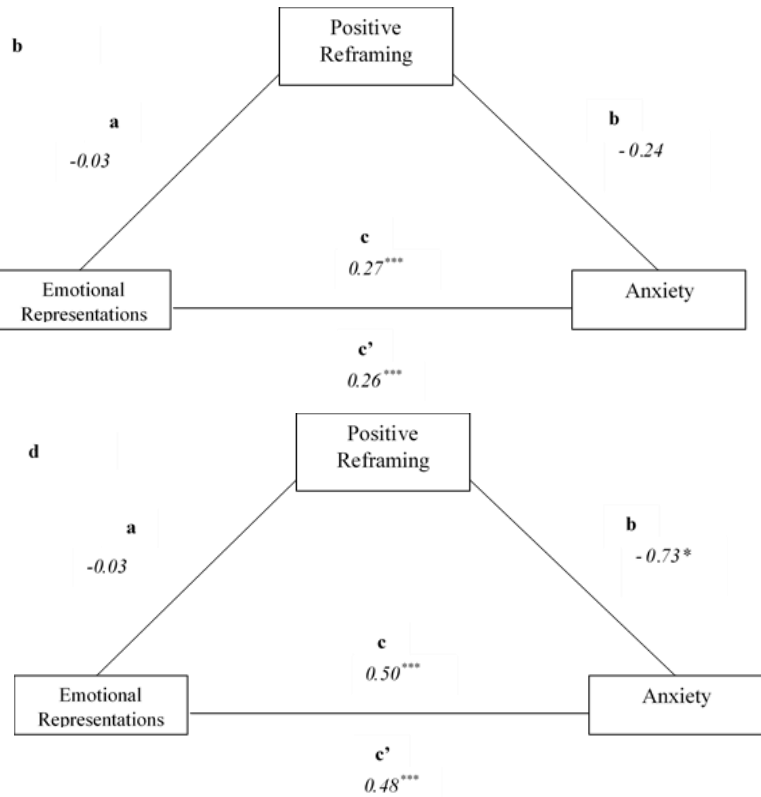
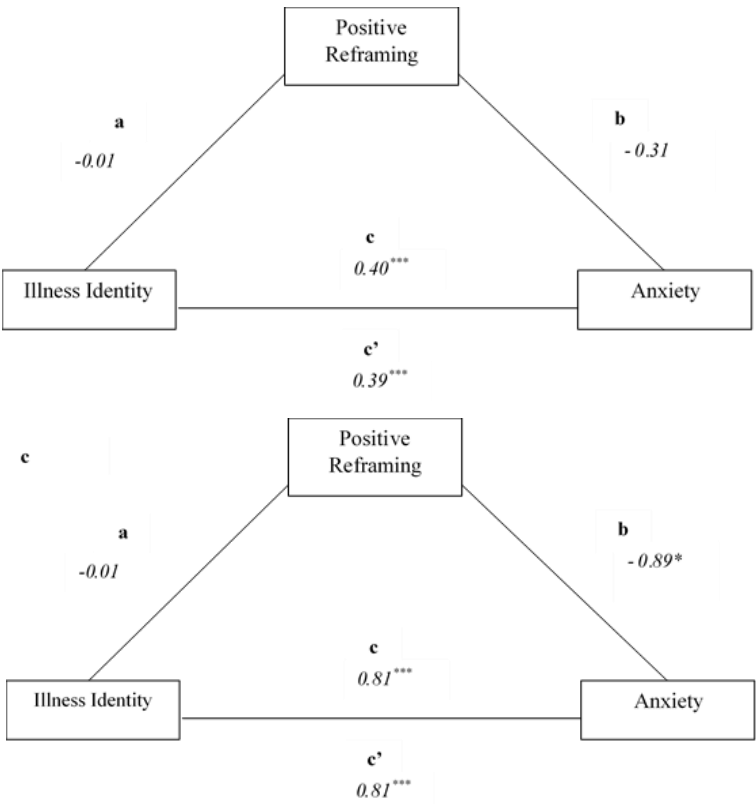
Appendix XI: Additional Factors and Outcome Correlational Analysis

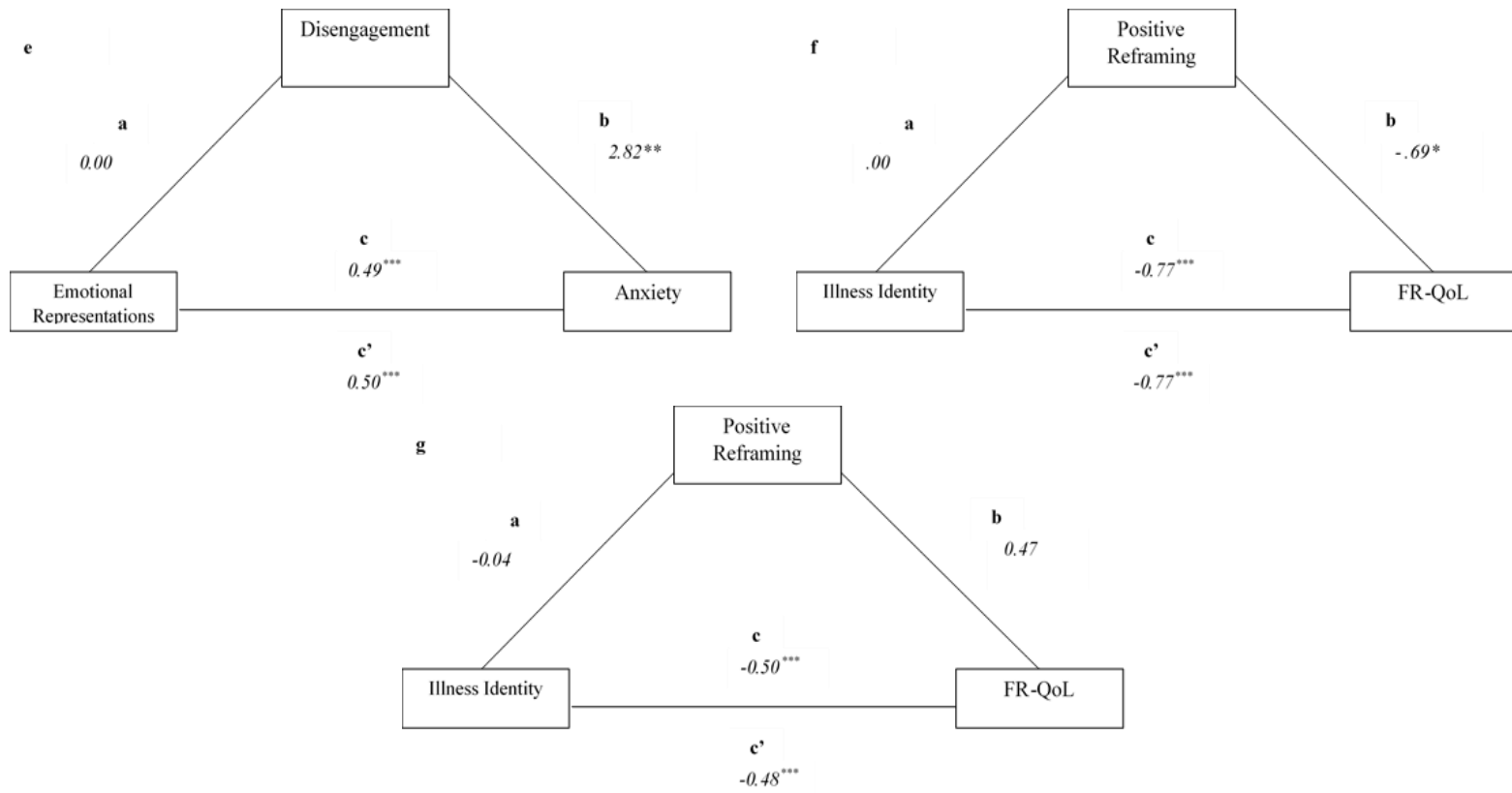
	1	2	3	4	5	6	7	8
1) HADS-A	1							
2) HADS-T	.913**	1						
3) SWFL	-.325**	-.388**	1					
4) WSAS	.358**	.467**	-.385**	1				
5) PHQ-15	.560**	.587**	-.407**	.552**	1			
6) PSS	.702**	.755**	-.415**	.408**	.500**	1		
7) IBS Total	.380**	.384**	-.427**	.461**	.667**	.342**	1	
8) PFI Severity	.184**	.163*	-.318**	.230**	.354**	0.096	.336**	1

**only correlations significant at 0.01 level (2-tailed) are shaded*

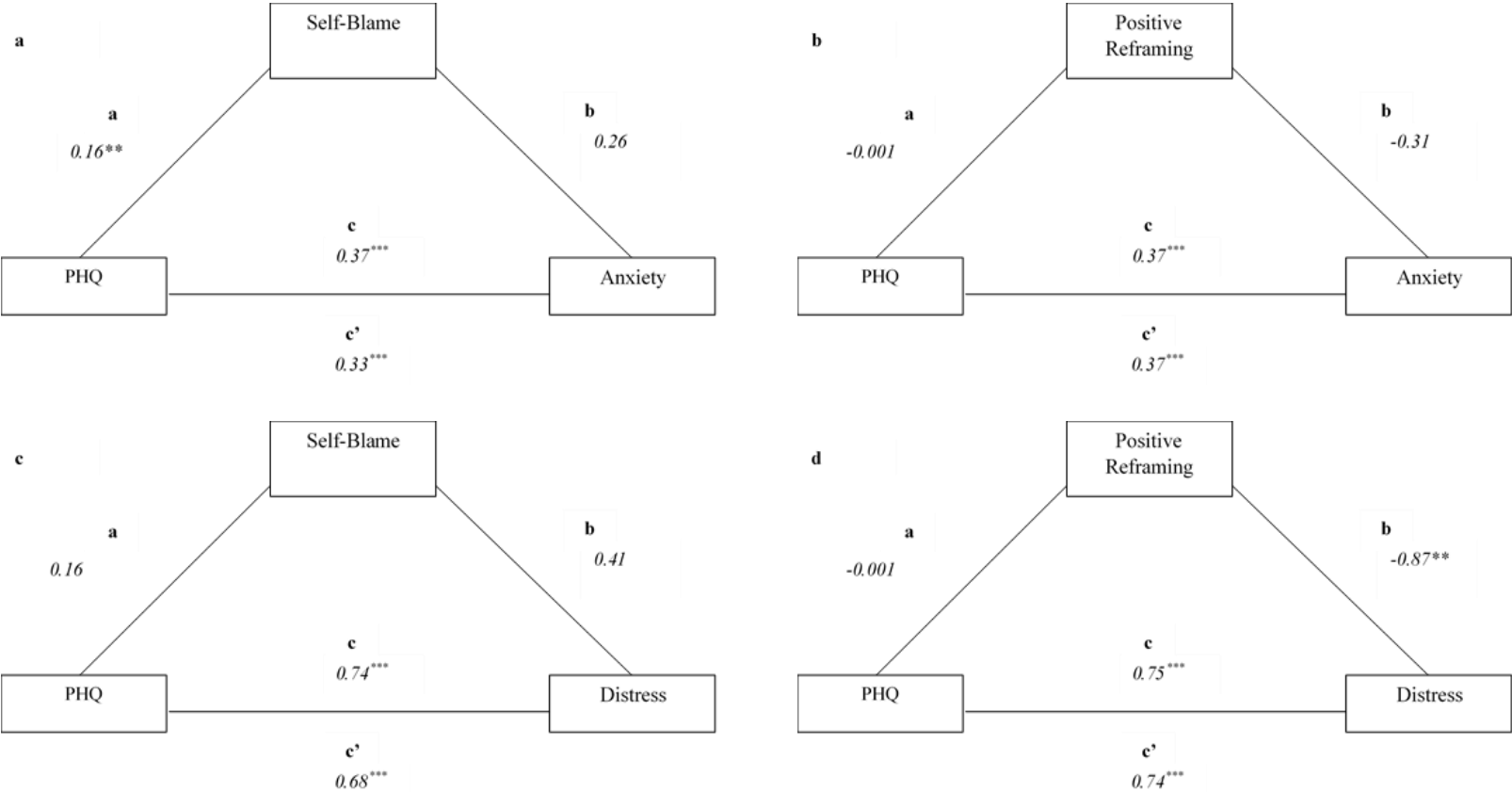


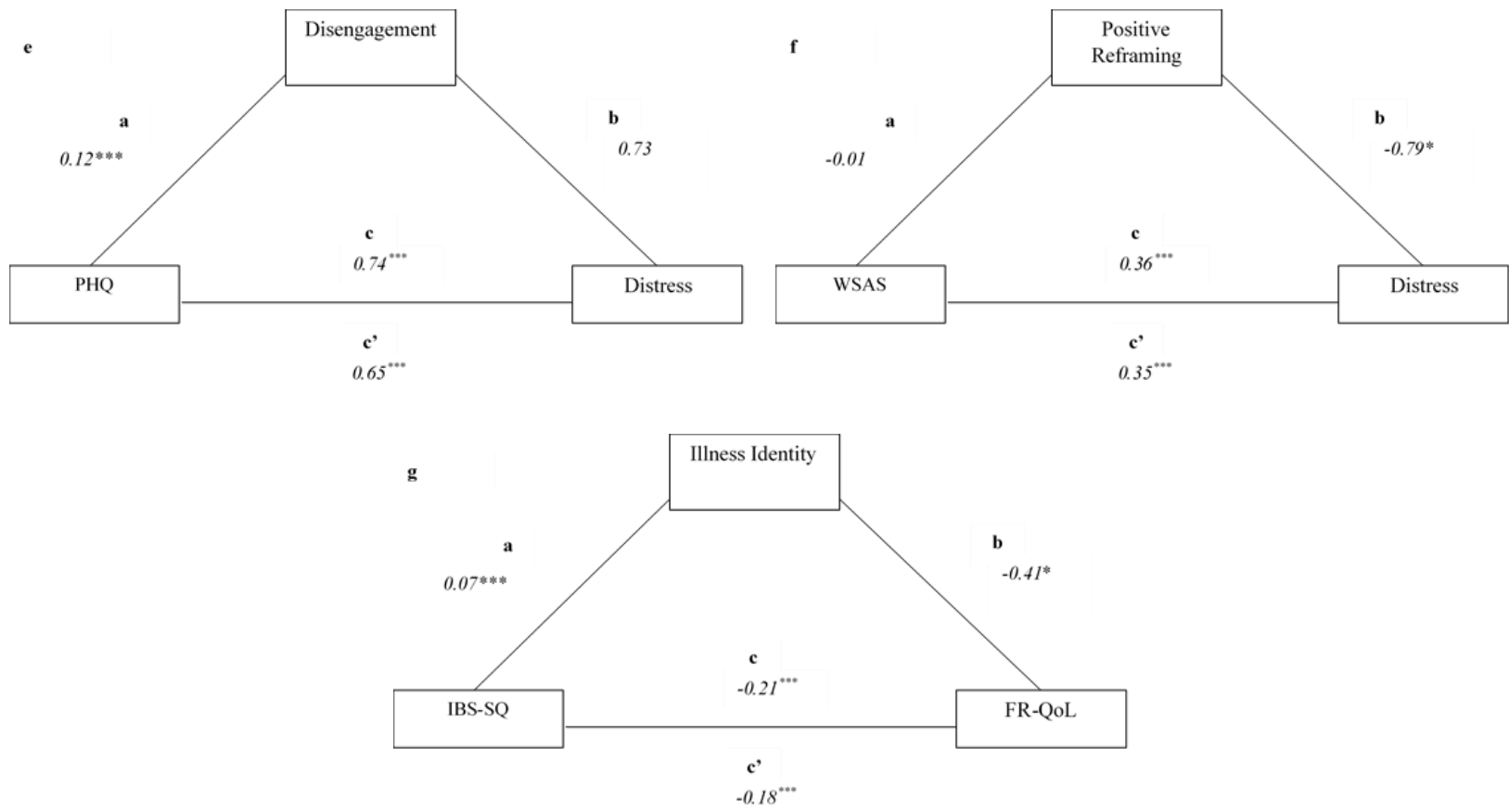
Appendix XII: CSM Mediation Models for Null Results





Appendix XIII: Additional Factors Mediation Models for Null Results





Appendix XIV: Proposed 4-session ACT Intervention

Session	Session Components	ACT Processes
Session 1	<p>- Discussion of why we are here and that the aim of the intervention is to work towards continuing to live a meaningful life and being able to engage in what matters most, alongside difficulties relating to PFI</p> <p>Psychoeducation:</p> <ul style="list-style-type: none"> - What is currently understood about PFI; symptoms experienced, unpredictability of symptoms and reactions, lack of diagnosis, treatment and/or cure and how people typically manage - The evolution of our brain to be 'on the lookout', and how this can contribute to vigilance, noticing symptoms, enhanced pain sensitivity, and anxiety - The gut-brain connection and the role of stress in contributing to the experience of GI symptoms - The connection between symptoms and the cognitive & emotional reaction to symptoms - The impact of food avoidance and reintroduction <p>Discussion Content:</p> <ul style="list-style-type: none"> - Explore what is currently done to cope with difficult thoughts, emotions and body sensations, and how well these strategies work in the short-term and long-term (creative hopelessness) <p>Experiential Components:</p> <ul style="list-style-type: none"> - Set personally meaningful goal to work towards during intervention - Passengers on a Bus metaphor - Mindful eating exercise <p>Between-Session Practice:</p> <ul style="list-style-type: none"> - 1 mindful eating practice each day 	<ul style="list-style-type: none"> - Self-as-context - Present moment awareness - Committed action

Session 2	<p>Discussion + Psychoeducation Content:</p> <ul style="list-style-type: none"> - Update on goal and progress towards it – problem solve as necessary. - Explore current cost of experiential avoidance (in relation to personal values and overall enjoyment of life) of trying to control these experiences & current cost of trying to maintain strict food avoidance. - Explore the paradoxical nature of control and what happens when things don't go as planned, or when difficult experiences are encountered. - Introduce the choice point and discuss what takes one away/towards what matters most - Explore role of self-blame and disengagement, and clarify if they take one towards what matters most or if these contribute to further suffering - Discuss the human nature of responses and how they are understandable, but sometimes are not helpful in the long term. Connect with idea about compassionate mind and how to foster compassion for self. - Additional goal setting exercise (long-term goal) <p>Experiential Components:</p> <ul style="list-style-type: none"> - Start with mindfulness exercise - Choice Point - Self-compassion exercise <p>Between-Session Practice:</p> <ul style="list-style-type: none"> - 1+ mindful eating practices each day - 1+ additional mindfulness practices each day - Create own Choice Point during the week 	<ul style="list-style-type: none"> - Present moment awareness - Acceptance - Values + Self-compassion
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Session 3	<p>Discussion + Psychoeducation Content:</p> <ul style="list-style-type: none"> - Update on goal and progress towards it – problem solve as necessary. - Explore willingness to experience an unpleasant symptom or a difficult emotion, followed by willingness practice and self-compassion following - Explore how the mind works, including the role of language, fusion and relational framing (e.g. how even hearing or seeing the ‘offending food’ can make one feel anxious or upset) <p>Experiential Components:</p> <ul style="list-style-type: none"> - Start with mindfulness exercise - Willingness exercise - Defusion exercise ‘I am having the thought that’ - Deliteralisation using the word of their food intolerance (e.g. milk) <p>Between-Session Practice:</p> <ul style="list-style-type: none"> - Continued daily mindfulness practice and mindful eating practice - Practice willingness each day and record how long tolerated - Continue creating own choice point and reflecting on what takes you away from and towards what matters most. 	<ul style="list-style-type: none"> - Present moment awareness - Defusion - Acceptance <p>+ Self-compassion</p>
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4	<p>Discussion + Psychoeducation Content:</p> <ul style="list-style-type: none"> - Explore what values and goals are, the importance of values and goals, and how they relate to each other - Clarifying values & exploring willingness and values in the context of goal-setting - Explore barriers to goals and what skills can be used from sessions so far to help flexibly adapt - Explore how one can commit to doing what matters in the context of difficulty, and what helpers we might need to support commitment to that goal - Explore self-compassion & perspective-taking exercise - Reflect on past four sessions and how to help bring ideas with you on your journey <p>Experiential Components:</p> <ul style="list-style-type: none"> - Start with mindfulness exercise - 80th birthday exercise (values) - Goal setting exercise - Self-compassion exercise - Declaration of committed action 	<ul style="list-style-type: none"> - Present moment awareness - Self-as-context - Values - Committed action <p>+ Self-compassion</p>
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—END—